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FIELD OF STUDY: BIOMECHANICS

DEPARTMENT OF ANATOMY AND BIOMECHANICS

DOCTORAL THESIS SUMMARY

NEURO BIOMECHANICAL PRINCIPLES IN ROBOT-ASSISTED GAIT TRAINING FOR PEDIATRIC PATIENTS

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ABSTRACT

Title: Neuro Biomechanical principles in robot-assisted gait training for pediatric patients

Background: There is a lack of data on how robot-assisted gait training (RAGT) contributes to gait changes in children with cerebral palsy (CP).

Methods: This research study investigated efficacy of a 4-week RAGT intervention in twelve ambulatory spastic diparesis children with CP (10.8±2.6 years old; 2 girls and 10 boys; Gross Motor Function Classification System I-III) by using computerized gait analysis (CGA); passive joint range of motion (PROM); selective control assessment of lower limbs evaluation (SCALE), and the six-minute walk test (6MWT). Pre-post RAGT intervention data of children with CP was compared with the normative data curves of typically developing children by cross-correlation, and further statistically evaluated by a Wilcoxon test.

Results: Significant pre-post RAGT intervention differences ($p<0.05$) that indicate more physiological gait comparing to the normative data curves were found. Biceps femoris, rectus femoris, and tibialis anterior decreased activity almost across all gait cycle phases. Medial gastrocnemius decreased activity mainly in terminal stance, mid-swing, and terminal swing phases. Internal hip rotations and foot progress angles decreased almost across all gait cycle phases. More economic energy expenditure was observed in spatiotemporal gait parameters. No significant changes were observed in kinetics. Decreased joint contractures were observed in all joints, except for the popliteal angles. SCALE scores improved by at least one point and children increased walked distance by 75 meters in the 6MWT.

Conclusion: The key findings of the research study suggest that RAGT as monotherapy can induce more physiological muscle activity and joint kinematics trajectories, more economic energy expenditure in spatiotemporal gait parameters, increased SVMC ability, walking farther distances, and decreased joint contractures in CP children with spastic diparesis.

Keywords: Cerebral palsy, motor control, gait, computerized gait analysis, robot-assisted gait training, Lokomat, joint range of motion, six-minute walk test

CONTENT

LIST OF USED ABBREVIATIONS

Biceps femoris (BF)

Body weight support (BWS)

Central nervous system (CNS)

Central pattern generator (CPG)

Cerebral palsy (CP)

Computerized gait analysis (CGA)

Center of pressure (COP)

Corticospinal tract (CST)

Cross-correlation (CC)

Effect size (ES)

Electroencefalograhpy (EEG)

Gait cycle (GC)

Gross Motor Function Classification System (GMFCS)

Ground reaction forces (GRF)

Initial contact (IC)

Initial swing (IS)

Less impaired limb (LIL)

Less impaired side (LIS)

Loading response (LR)

Magnetic resonance imaging (MRI)

Medial gastrocnemius (MG)

Midstance (MDST)

Midswing (MSW)

More impaired limb (MIL)

More impaired side (MIS)

Normalized cross-correlation (NCC)

Passive range of motion (PROM)

Principal investigator (PI)

Pre-swing (PSW)

Range of motion (ROM)

Rectus femoris (RF)

Robot-assisted gait training (RAGT)

Selective Voluntary Motor Control (SVMC)

Selective Control Assessment of the Lower Extremity (SCALE)

Six-minute walk test (6MWT)

Spatiotemporal parameters (STP)

Surface EMG for Non Invasive Assessment of Muscles (SENIAM)

Surface electromyography (sEMG)

Tibialis anterior (TA)

Terminal stance (TS)

Terminal swing (TSW)

Therapy protocol (TP)

University Rehabilitation Institute of Republic Slovenia - Soča (URIS)

1. INTRODUCTION

Cerebral palsy (CP) represents arguably the most common congenital disorder often used to describe a group of syndromes that develop due to pre-existing damage or disturbances in the developing brain. CP affects motor control resulting in a limited activity that is attributed to non-progressive disturbances occurring in the fetal or infant brain. Furthermore, CP can manifest into various levels of sensory, mental, or other developmental deficits, which are most likely non-progressive, but often varying during the child's development. Children with CP benefit from intensive physiotherapy enhancing motor development to achieve independent walking. Although some forms of CP can achieve independent or partially independent walking, walking manifests itself as pathological accompanied by a lack of selective voluntary motor control, restricted joint range of motion, spasticity, and inability to walk farther distances. According to the latest research, task-specific training and physiotherapy induce functionally relevant plastic changes in the brain, and it seems to be an effective way of addressing motor symptoms, as brain plasticity in the human locomotor networks seems to be task-dependent. Robot-assisted gait training (RAGT) is considered one form of task-dependent training which enhances the motor development of children with CP. Although manual assistance can be used to aid children with CP, RAGT allows for more advanced and customizable gait rehabilitation programs. RAGT consists of bilateral robotic orthoses, body-weight support (BWS), and a treadmill. Being a computerized system, it is possible to adjust the amount of BWS to maintain extended posture and provide accurate loading of the lower limbs. The robotic orthoses guide a patient's leg movements throughout repeatable predefined trajectories of lower extremities.

Considering the structure and function of RAGT devices, the main aim of RAGT is to improve the motor learning process through repetitive stimulation of gait accompanied by audio-visual feedback RAGT provides a simplified and safe therapeutic environment that allows for prolonged training duration with many repetitions of steps, while inducing a reproducible, kinematically consistent, symmetrical gait pattern.

Figure 1: A 5-year-old boy with spastic diparesis during RAGT using the Lokomat Pro (source: own).

2. METHODS

2.1. Study design

An empirical quantitative evaluation form of the research study using descriptive statistics to explain causalities and consequences among individual variables (Hendl, 2016).

2.2. Aim of the research study

The purpose of this research study was to investigate the effects of a 4-week RAGT intervention as monotherapy on the quality of gait patterns in spastic diparesis children with CP.

2.3. Scientific question and hypotheses

Can RAGT induce a more physiological gait in ambulatory children with CP that would be comparable with healthy children?		Method used to confirm/reject hypothesis
H0	The gait pattern of children with CP will remain unchanged following RAGT intervention.	All procedures
H1	RAGT will induce a more physiological sEMG muscle activity by the means of approximation to the normative curve.	CGA - sEMG
H2	RAGT will induce more physiological joint kinematics trajectories by the means of approximation to the normative curve.	CGA - joint kinematics
H3	RAGT will induce more physiological gait kinetics by the means of approximation to the normative curve.	CGA - kinetics
H4	RAGT will enhance the ability of children with CP to walk farther distances.	CGA - spatiotemporal parameters, 6MWT
H5	Children with CP will increase the PROM in all joints following RAGT intervention.	Clinical tests - PROM
H6	Children with CP will show a higher ability to perform selective movements of hip, knee, and ankle joint following RAGT intervention.	Clinical tests - SCALE

Table 1: Overview of scientific question and individual hypotheses.

2.4. Inclusion criteria of the research study

Inclusion criteria were: CP type spastic diparesis; Gross Motor Function Classification (GMFCS) I-III; ability to walk independently for at least short distances; femur length at least 21 cm; age 5–15 years; ability to communicate fear, pain, or discomfort; ability to follow simple instructions; no botulinum toxin in the last 3 months before RAGT; no orthopedic surgical intervention in the last 12 months; no anti-spastic medications; no severe contractures; and ability to attend 20 RAGT sessions scheduled in 20 consecutive weekdays (Meyer-Heim et al., 2009; Schuler et al., 2011; Meyer-Heim and van Hedel, 2013; Vrečar, 2013; Beretta et al., 2015; Wallard et al., 2017, Beretta et al., 2020).

2.5. Data collection

As this study aimed to explore effects followed by RAGT which include an extensive amount of variables, the data collection was divided into two parts:

- CGA in the gait laboratory
- reliable, valid, and standardized clinical evaluations

The combination of the CGA and clinical evaluations allows for a comprehensive interpretation of gait pathologies in children with CP. Methods were chosen based on the latest literature research and PI's own empirical experience. This research study used standardized, valid, and reliable methods that are routinely used in the assessment of children with CP. CGA (Wren et al., 2011), PROM (Nordmark et al., 2009), and 6MWT (Thompson et al., 2008) are the most frequently used in clinical decision-making, and monitoring outcomes following therapeutic or surgical interventions in children with CP. Additionally, this research study included the tool for SVMC assessment - SCALE (Fowler, 2009).

2.6. Procedures

All children with CP enrolled in the research study were treated as out-patients, and following procedures were covered by the Slovenian healthcare insurance system. All children with CP were evaluated in the same gait laboratory and same premises of the children's rehabilitation department at URIS. Data was collected by following standardized protocols for both clinical and gait analysis procedures. All procedures were performed in the exactly same order before and after completing the 4-week RAGT intervention. A detailed description of procedures and RAGT intervention follows.

2.6.1. Computerized gait analysis

The CGA was performed in the Kinesiology and Biomechanical Laboratory of URIS by the PI, two same physiotherapists, and two biomechanics experts. The CGA included 3D gait analysis consisting of joint kinematics, kinetics, sEMG, and spatiotemporal parameters.

Anthropometry

First, all children with CP were measured weight, height, leg length, knee and ankle joints circumferences (Baker, 2013). This data was further used by biomechanics experts for data processing.

Placement of sEMG electrodes

The skin of children with CP was gently abraded, and 3M Red Dot 2560 & 2570 Multi-purpose Monitoring Electrodes were placed on the following muscles bilaterally according to the SENIAM recommendations (Hermens et al., 2000): tibialis anterior (TA), medial gastrocnemius (MG), rectus femoris (RF), and biceps femoris (BF). A neutral reference electrode was attached to the tensor fascia latae muscle (Schuler et al., 2011). A multimeter was used to evaluate the values of skin resistance. Values between 0-10 Ohm were considered sufficient, whereas values over 10 Ohm were considered too high. If needed, the skin preparation procedure was repeated to assure proper skin resistance and electrode attachment (Hermens et al., 2000; Baker, 2013).

Placement of reflective markers

Subsequently, 17 reflective markers (Vicon, Oxford Metrics, Oxford, UK) were attached directly to the skin of children with CP. Markers were attached bilaterally to the following body areas concerning the Vicon Plug-in-Gait biomechanics model (Davis et al., 1991): second metatarsal joint; middle of the Achille´s tendon; malleolus lateralis; center of the tibia; lateral femoral epicondyle; lateral side of the thigh; spina iliaca anterior superior (SIAS); L5; Th10; sternum.

CGA data collection

Biomechanics experts calibrated the VICON camera system (0.3 MPix VICON, Oxford Metrics, Oxford, UK) before the data collection. All children with CP were told to walk barefoot in the pre-designed 10-meter flat-surface pathway to adapt to space. Subsequently, children with CP were supposed to stay still in the center of the AMTI force plates (AMTI OR6) in an anatomical position so that biomechanics experts could record the neutral position of all body segments. Afterward, children with CP were appealed to walk barefoot without walking aids at preferred speed and according to physical capacities for a minimum of ten trials on the same pre-designed 10-meter flat-surface pathway in the gait laboratory. Kinematics, kinetics, and sEMG data were collected and recorded simultaneously. 3D kinematic data was recorded by using a 6-camera VICON system (0.3 MPix VICON, Oxford Metrics, Oxford, UK) with a sampling frequency of 50 Hz until the course of three completed trials was obtained. Kinetics was recorded by using AMTI force plates (AMTI OR6, Advanced Mechanical Technology Inc., Watertown, MA) at 1 kHz sampling frequency. Muscle activity was recorded with an 8-channel sEMG sampling frequency at 1 kHz (Noraxon TeleMyo 2400T, Noraxon U.S.A. Inc.).

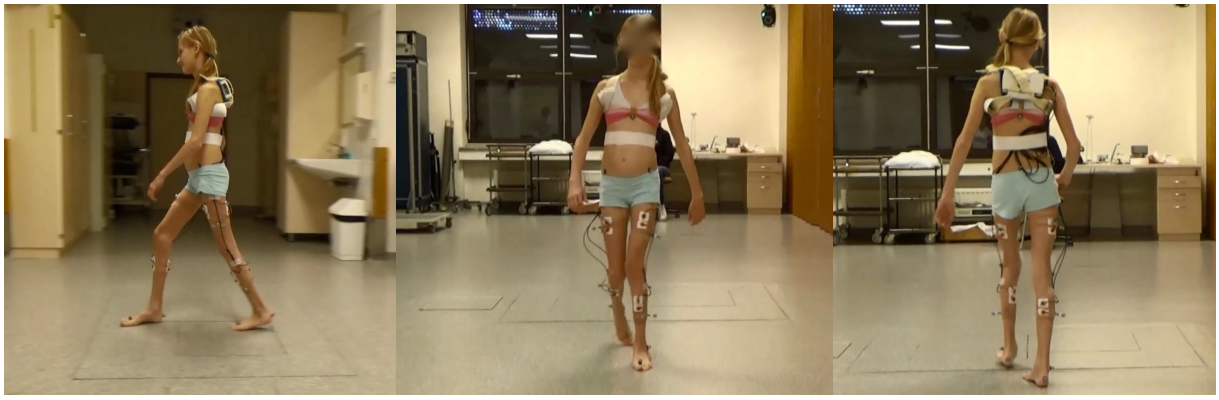

Figure 2: An 11-years-old girl with CP during CGA (source: own).

2.6.2. Clinical tests

All clinical tests were performed by the PI and senior pediatric physiotherapist from Children's rehabilitation department.

Passive joint range of motion

PROM is a routinely used assessment that informs about the passive range of motion of particular joints and the presence of contractures (Kilgour, 2003). The assessment was always performed by two same assessors (the PI and senior pediatric physiotherapist). One assessor measured the range of motion using a standardized plastic goniometer (McWhirk et al., 2006). Another assessor performed the passive movement and fixation of the child's lower limb. All children with CP were asked to relax assessed lower limb, and remain passive during the evaluation. The assessor passively moved lower limb joints into such a position until the maximum joint barrier occurred, and this value was recorded in the score sheet. A detailed description of the PROM procedure follows.

Hip joint extension

Children with CP were assessed in a supine position with fixed lumbar lordosis to keep the pelvis in a neutral position and to prevent an error during measurement. The untested leg was flexed whilst the tested leg was passively moved from maximal flexion to extension. Goniometer was attached to trochanter major to measure the angle between the trunk and the thigh. The physiological value is zero degrees. Values ranging between 0–20° mean that hip flexor contracture is present; values ranging between 0 to -15° mean that hip flexors are stretched (Katz, et al., 1992; Nordmark, 2009).

Hip joint rotations

Children with CP were assessed in a prone position with a fixed pelvis to prevent anteversion. The tested leg was passively moved to internal and subsequently external rotations. A goniometer was attached to the center of the patella to measure the angle between the knee and shin bone. The physiological value is 45° for each of the rotations (Katz, et al., 1992; Nordmark, 2009).

Knee joint extension

Children with CP were assessed in a supine position with fixed lumbar lordosis to keep the pelvis in a neutral position to prevent an error during measurement. The untested leg was flexed whilst the tested leg was passively moved from maximal knee flexion to extension. A goniometer was attached to the lateral epicondyle of the femur to measure the angle between the thigh and shin bone. The physiological value is 180°. Values ranging between 0–20° mean that hamstring contracture is present; values ranging between 0 to -10° or even more mean that knee hyperextension is present (Katz, et al., 1992; Nordmark, 2009).

Popliteal angles

Children with CP were assessed in a supine position to evaluate the hamstring contracture. Lumbar lordosis was fixed to keep the pelvis in a neutral position and to prevent an error during measurement. Both unilateral and bilateral popliteal angles were measured and the goniometer was attached to the lateral femoral epicondyle. Physiological values are 180° for bilateral and 130° for unilateral popliteal angles (Katz, et al., 1992; Berge et al., 2007).

Ankle joint dorsal flexion

Children with CP were assessed in a supine position. The measurement was performed with flexed and extended knee joint. In both measurements, the goniometer was attached to the medial malleolus to measure the angle between shinbone and foot. Physiological values range between 30–40° (Katz, et al.).

Selective Control Assessment of The Lower Extremity

SCALE test was used to assess the selectivity of movements in the hip, knee, ankle, subtalar joint and fingers. Detailed description of examined joints and positions is described below (Fowler et al., 2009; Fowler et al., 2010).

Hip joint

The hip joint was assessed in a side-lying position with the hip and knee fully extended. The tested limb was supported medially at the knee and ankle. For better stability, the untested limb was flexed. The tested motion is hip flexion while keeping the knee extended. Children with CP were asked to flex, extend then flex the hip while keeping the knee extended.

Knee joint

Children with CP were in a sitting position with the legs over the edge of the exam table. Children with CP were asked to extend, flex then extend the knee while keeping the hip flexed.

Ankle joint

Children with CP were in a sitting position with the legs over the edge of the exam table. The knee joint was extended and the assessor supported the calf. Children

with CP were asked to dorsiflex, plantar flex then dorsiflex the ankle while maintaining knee extension.

Foot/subtalar Joint

Children with CP were in a sitting position with the legs over the edge of the exam table. The knee joint was extended and the assessor supported the calf. Children were asked to invert, evert then invert while maintaining knee extension.

Toes

Children with CP were in a sitting position with the legs over the edge of the exam table. The knee joint was extended and the assessor supported the heel. Children were asked to flex, extend then flex toes without moving ankle or knee.

Six-minute walk test

Timed 6MWT assessed the maximum walked distance in 6 minutes. This test was performed in a non-distracting environment of a 100-meter long corridor that was intended for walk tests at the rehabilitation department of URIS. All children with CP wore comfortable footwear as well as orthoses if regularly used. All children with CP were told to walk at a self-selected speed that they typically use for long walks and avoid talking. Running or faster walking was not allowed during the test. Both assessors were present and provided encouragement to keep children with CP engaged in the task for full 6 minutes (de Groot and Takken, 2011). The total distance walked was recorded.

2.6.3. Definition of limb impairment

SCALE and PROM evaluations defined the more and less affected lower limb. These were administered as “more impaired limb” (MIL) and “less impaired limb” (LIL). (Fowler et al., 2009; Syczewska and Świecicka, 2016).

2.7. Robot-assisted gait training intervention

The RAGT was performed by the PI under the supervision of the senior pediatric physiotherapist from Children’s rehabilitation department. Therapy protocol (TP) consisted of twenty sessions scheduled for 20 consecutive workdays with a minimum duration of 30 and up to a maximum of 45 minutes (Vrečar et al., 2013; Wallard et al., 2017). Therapy duration was increased progressively by at least 3 minutes every other day. All children with CP walked with augmented feedback that comprised of a motivational video game (Schuler et al., 2011; Schuler et al. 2013; Wallard et al., 2017). The treadmill speed was synchronized with the movements of the robotic orthoses and set to a comfortable walking speed of every child individually. These parameters were set by following the child’s ability to walk at a certain speed, follow the augmented feedback and maintain an upright posture. All children wore shoes during the TP. At the beginning of the RAGT program, all children had an initial level of BWS set to 50% of body weight (Schuler et al., 2013). The BWS was further decreased for every child individually until the knee started to collapse into flexion during the stance phase due to the increased load of body weight. All children walked with augmented biofeedback. For consistency, the PI was present at every RAGT session to follow the progression, encourage the child to walk actively, and keep an extended posture (see Figure 7).

2.8. Data evaluation

2.8.1. CGA data processing

The CGA data was processed by two biomechanics experts from Kinesiology and Biomechanical Laboratory at URIS that followed standardized guidelines for data processing. Raw CGA data obtained from overground gait was high-pass filtered by the VICON system (VICON Nexus 1.8.3.) to enable analog data sampling with 1 kHz, and subsequently filtered with a 4th order low-pass Butterworth filter with a cut off frequency of 20 Hz (Kadaba et al., 1989; Baker, 2013). The data was normalized and the Vicon Plug-in-Gait model was used to generate kinematic and kinetic data (Davis et al., 1991). Joint angles were calculated based on 3D coordinates of markers. Internal joint moments and power were calculated based on joint kinematics and ground reaction forces recorded using force plates (Kadaba et al., 1989; MacWilliams et al., 2003; Baker, 2013). Force plates measured ground reaction forces and center of pressure (COP) trajectory (Baker, 2013). VICON Nexus 1.8.3. and Polygon 3.5.1. softwares (VICON, Oxford Metrics, Oxford, UK) were used to define the gait cycles, spatiotemporal parameters, joint angles, internal joint moments, and power. sEMG data was processed by MyoResearch XP 1.07 Master Edition software (Noraxon Inc., Scottsdale/USA). Raw sEMG signals were high-pass filtered with a bi-directional zero-lag Butterworth at a cut-off frequency of 10 Hz, rectified, and smoothed with a time window of 100 ms to create the linear envelope. The sEMG data was normalized to the maximum EMG recorded during the gait cycle (Fung et al., 1989; Burden and Bartlett, 1999; Burden et al., 2003; Bojanic et al., 2011; Aurich-Schuler, 2017; Ricklin et al., 2018). As subjects walked for a minimum of ten trials, gait cycles were identified in each trial. Heel strike and toe-off markers were set automatically by the software program and adjusted manually if necessary.

The gait cycle starts and ends with a heel strike of the same lower extremity (Perry, 2010; Baker, 2013). Within the cycles, the mean value of these trials was calculated to obtain 1 gait cycle and separate gait phases. The gait cycle was represented by 51 evenly spaced samples (0–100% in 2% steps). As this study aimed to explore whether RAGT can induce physiological gait changes in lower limbs that will be comparable to the healthy children, a comparison of all CGA variables was made with normative data curves from typically developing children (Hof et al., 2005; Winter, 2009). Normative data are an integral part of VICON and Myoresearch softwares. Subsequently, detailed gait analysis reports were generated by the software for every child individually together with the detailed overview of all variables in the .csv format datasheets. Gait analysis report data sheets including all kinematics, kinetics, sEMG, and spatiotemporal variables were used for statistical evaluation.

2.8.2. Statistical evaluation of CGA data

The statistical evaluation of CGA data was done by the PI in cooperation with a biomechanics expert from the Faculty of biomedical engineering, CTU. Data were evaluated by a custom-written MatLab program (MatLab software processes, MatLab R2010b, Mathworks, Inc., Natick, MA, USA). The following variables from the gait analysis report data sheets were prepared for statistical evaluation (see Table 2).

Group of variables (units of measurement)	List of variables (MIL, LIL)
sEMG signals (V)	biceps femoris, rectus femoris, medial gastrocnemius, tibialis anterior
3D joint kinematics (degrees)	pelvis, hip, knee, ankle, thorax tilt
kinetics (N)	hip, knee and ankle joints power and moments ground reaction forces (GRF) center of mass (COM) center of pressure (COP)

Table 2: Overview of variables from gait analysis report; *Legend:* Computerized gait analysis (CGA); More impaired limb (MIL); Less impaired limb (LIL).

A 5-step statistical analysis was done as follows:

1) *calculation of the deviation of CP signals from the normative values of healthy children for all CGA variables by using normalized cross-correlation (NCC)*
2) *verification of data normality distribution*
3) *comparison of condition pre- and post-RAGT intervention by using Wilcoxon sign rank test*
4) *calculation of effect sizes*
5) *calculation of dependencies among selected pairs of variables by using Spearman correlation*

First, gait cycle phases were identified according to Perry (2010) as: 0-2% initial contact; 2-12% loading response; 12-31% midstance; 31-50% terminal stance; 50-62% pre-swing; 62-75% initial swing; 75-87% midswing; 87-100% terminal swing. Subsequently, the deviation of CP signals from the normative values of healthy children (Hof et al., 2005; Winter, 2009) was calculated by normalized cross-correlation (NCC) for every child with CP (Mahaki et al., 2017; Kaso, 2018), every CGA variable, and for all gait cycle phases. This calculation was performed for MIL/LIL separately, and pre- and post-RAGT intervention to obtain twelve values of NCC “pre-intervention” and “post-intervention”. Finally, the median value of twelve CP children NCC was calculated and further statistically compared. The NCC was followed by the statistical evaluation that aimed to compare the pre- and post-intervention conditions of all children with CP. The Shapiro-Wilk test was used to verify data normality (Cohen, 1988). As normal data distribution has been rejected at the 0.05 significance level, the non-parametric Wilcoxon sign rank test (Cohen, 1988) was used for further statistical calculation of each variable at the 0.05 significance level. Furthermore, the Wilcoxon sign rank test was completed with the calculation of effect sizes where large effect was 0.5, a medium effect was 0.3, and a small effect was 0.1 (Cohen, 1988, Fritz et al., 2012). Finally, Spearman correlation was used to evaluate dependencies among selected pairs of variables (see Table 3 and Table 4).

Pairs of kinematics/kinetics variables (MIL, LIL)
pelvic tilt / knee flexion extension (°)
hip flexion extension / knee flexion extension (°)
knee flexion extension / ankle flexion extension (°)
hip rotation / knee abduction adduction (°)
hip abduction adduction / knee abduction adduction (°)
thorax tilt / pelvic tilt (°)

Table 3: Pairs of kinematics/kinetics variables; *Legend:* More impaired limb (MIL); Less impaired limb (LIL).

Pairs of sEMG variables for Spearman correlation (MIL, LIL)
RF / BF (V)
MG / TA (V)

Table 4: Pairs of sEMG variables; *Legend:* More impaired limb (MIL); Less impaired limb (LIL).

Spearman's rank correlation coefficient was used as normal data distribution has been rejected, A large correlation was 0.5, medium was 0.3 and small was 0.1 (Cohen, 1988). Additionally, the non-parametric Wilcoxon sign rank test was used to compare the pre- and post-intervention spatiotemporal variables (see Table 5) at the 0.05 significance level (Cohen, 1988).

Spatiotemporal parameters
cadence (steps/min)
double support (seconds)
foot off (%)
opposite foot contact (%)
opposite foot off (%)
single support (seconds)
step length (meters)
step time (seconds)
step width (meters)
stride length (meters)
stride time (second)
walking speed (meter/second)

Table 5: Spatiotemporal parameters.

2.8.3. Data processing of clinical tests

Clinical tests were processed by the PI. Pre- and post-RAGT intervention results of PROM angles, SCALE scores, and total distance walked in 6MWT were recorded in the score sheets and compared with normative values from typically developing children. Finally, the differences of ‘pre-intervention and normative’ and ‘post-intervention and normative’ conditions were calculated for every clinical test separately. The difference values of PROM, SCALE, and 6MWT tests were further statistically evaluated by using a custom-written MatLab program (MatLab software processes, MatLab R2010b, Mathworks, Inc., Natick, MA, USA).

2.8.4. Statistical evaluation of clinical tests

The statistical evaluation of clinical tests was done by the PI in cooperation with a biomechanics expert from the Faculty of biomedical engineering, CTU. A custom-written MatLab program (MatLab software processes, MatLab R2010b, Mathworks, Inc., Natick, MA, USA) was used. The following data sets for each of the MIL and LIL variables were prepared (see Table 6).

PROM (degrees) MIL, LIL	**SCALE score MIL, LIL**	**6MWT**
Hip joint extension	Hip joint	Total distance walked pre-RAGT intervention
Hip joint rotations	Knee joint	Total distance walked post-RAGT intervention
Knee joint extension	Ankle joint	
Popliteal angles	Foot/Subtalar joint	
Ankle joint dorsal flexion	Toes	

Table 6: Overview of clinical tests and variables; *Legend:* Passive range of motion (PROM); Selective Control Assessment of Lower Extremities (SCALE); Six-minute walk test (6MWT); More impaired limb (MIL); Less impaired limb (LIL).

The statistical evaluation was performed to compare the pre- and post-intervention patients' conditions. The Shapiro-Wilk test was used to verify data normality (Cohen, 1988). As normal data distribution has been rejected at the 0.05 significance level, the non-parametric Wilcoxon sign rank test (Cohen, 1988) was used for further statistical calculation of MIL and LIL separately (0.05 significance level). Furthermore, the non-parametric Wilcoxon sign rank test was completed with the calculation of effect sizes where large effect was 0.5, a medium effect was 0.3, and a small effect was 0.1 (Cohen, 1988, Fritz et al., 2012).

3. RESULTS

3.1. Children with cerebral palsy

Twelve CP children with spastic diparesis (10.8±2.6 years old; 2 girls and 10 boys; GMFCS I-III) met all inclusion criteria and completed the RAGT program. The program was well-tolerated by all of the children and no adverse events were reported. The baseline data are summarized in Table 7.

Patient ID and gender	Age (years)	GMFCS level	Walking pattern	Lokomat orthoses
1F	11	II	Toe walking	A
2F	11	III	Crouch gait with dominantly spastic hip adductors	P
3F	15	III	Crouch gait	A
4M	5,5	III	Toe walking	P
5M	7	II	Toe walking	P
6M	8	III	Crouch gait	P
7M	9	I	Toe walking	P
8M	9	II	Toe walking	P
9M	10	II	Toe walking	P
10M	11	I	Toe walking	A
11M	12	II	Toe walking	A
12M	16	II	Toe walking	A

Table 7: Baseline data of children with CP. In total twelve children with CP (10.8±2.6 years old; 2 girls and 10 boys; GMFCS I-III) were enrolled. 9 children had toe walking pattern, 3 children walked in a crouch gait (Sutherland et al., 1993). *Legend:* M (male); F (female); GMFCS (Gross Motor Functional Classification Score); A (adult); P (pediatric).

3.2. Intervention

All children underwent 20 RAGT sessions. On average, the RAGT sessions were 39±6 minutes long, and the average walking speed was 1.4±2.38 km/h. The average distance walked during a single RAGT session was 969±172 meters with an average BWS of 14.8±4.76 kgs.

3.3. CGA results

Significant pre-post RAGT intervention differences ($p<0.05$) that indicate more physiological gait according to the normative data curves were found (Hof et al., 2005; Winter, 2009).

3.3.1. sEMG results

As this study enrolled CP children with spastic diparesis, the significant improvement was found mainly in bilaterally decreased muscle activity. BF and RF muscles decreased activity almost across all gait cycle phases. MG decreased activity mainly in terminal stance, midswing, and terminal swing phases. TA showed decreased activity almost in all phases except for terminal stance and midswing. In general, small to moderate effect sizes could be found in the sEMG analysis ranging between 0.40032-0.6245 (see Table 8). Table 8 summarizes sEMG quantitative changes including effect sizes for all children with CP. Examples of qualitative changes in sEMG activity together with normative data curves from typically developing children are shown in Figures 16-19. BF/RF MIL agonist-antagonist pair showed a significant correlation in terms of their physiological muscle co-activation in the terminal stance, pre-swing, initial swing, and midswing phases. The only significant correlations in LIL were found in the midstance and terminal stance phases. MG/TA agonist-antagonist pair showed a significant correlation in terms of their physiological muscle co-activation in initial swing and midswing phases. In general, moderate to large correlations could be found in the sEMG agonist-antagonist pairs ranging between 0.503497-0.874126 (see Table 9). Table 9 summarizes sEMG agonist-antagonist pairs quantitative changes for all children with CP.

sEMG	Gait phase (p-value) / *Effect size*							
	IC	LR	MST	TS	PSW	ISW	MSW	TSW
BF MIL	0,007649	0,009633	0,00604	0,004742	0,00604	0,012063	0,009633	0,00604
ES	*0,544436*	*0,528423*	*0,560449*	*0,576461*	*0,560449*	*0,51241*	*0,528423*	*0,560449*
BF LIL	0,012792	0,020795	0,009633	0,004742	0,071189	0,002218	0,041389	0,004742
ES	*0,508168*	*0,47187*	*0,528423*	*0,576461*	*0,368295*	*0,6245*	*0,416333*	*0,576461*
RF MIL	0,003702	0,004742	0,002218	0,003702	0,002218	0,012063	0,00604	0,002873
ES	*0,592474*	*0,576461*	*0,6245*	*0,592474*	*0,6245*	*0,51241*	*0,560449*	*0,608487*
RF LIL	0,003346	0,002873	0,002873	0,002218	0,307821	0,03417	0,03417	0,012063
ES	*0,598912*	*0,608487*	*0,608487*	*0,6245*	*0,208167*	*0,432346*	*0,432346*	*0,51241*
MG MIL	0,022909	0,084379	0,03417	0,028056	0,03417	0,084379	0,018603	0,028056
ES	*0,464372*	*0,352282*	*0,432346*	*0,448359*	*0,432346*	*0,352282*	*0,480384*	*0,448359*
MG LIL	0,050461	0,075368	0,084379	0,041389	0,059739	0,009633	0,009633	0,04986
ES	*0,399275*	*0,362977*	*0,352282*	*0,416333*	*0,384308*	*0,528423*	*0,528423*	*0,40032*
TA MIL	0,022909	0,018603	0,084379	0,059739	0,03417	0,04986	0,157939	0,03417
ES	*0,464372*	*0,480384*	*0,352282*	*0,384308*	*0,432346*	*0,40032*	*0,288231*	*0,432346*
TA LIL	0,003346	0,002218	0,002873	0,002218	0,007649	0,007649	0,028056	0,009633
ES	*0,598912*	*0,6245*	*0,608487*	*0,6245*	*0,544436*	*0,544436*	*0,448359*	*0,528423*

Table 8: sEMG results. The deviation of CP signals from the sEMG normative values (Hof et al., 2005; Winter, 2009) of each variable was calculated by cross-correlation for every child's LIL and MIL separately pre- and post-intervention. Afterward, cross-correlation values 'pre-post intervention' were compared by using the Wilcoxon sign rank test. This table shows an overview of Wilcoxon sign rank test (p-value) results, including effect sizes for all variables across gait phases. Statistically significant results ($p<0.05$) are marked with yellow color. *Legend: ES* (effect size); More impaired limb (MIL); Less impaired limb (LIL); Initial contact (IC); Loading response (LR); Midstance (MST); Terminal stance (TS); Pre-swing (PSW); Initial swing (ISW); Midswing (MSW); Terminal swing (TSW); BF (biceps femoris); RF (rectus femoris); TA (tibialis anterior); MG (medial gastrocnemius).

sEMG correlations	Gait phase (rho value)							
	IC	LR	MST	TS	PSW	ISW	MSW	TSW
BF/RF MIL	-0,02797	-0,11189	0,48951	0,65035	0,874126	0,811189	0,657343	0,314685
BF/RF LIL	0,335664	0,384615	0,783217	0,853147	0,384615	0,342657	0,377622	0,454545
MG/TA MIL	0,475524	0,524476	0,391608	0,20979	0,363636	0,72028	0,503497	0,370629
MG/TA LIL	0,251748	0,335664	0,307692	0,286713	0,377622	0,251748	0,629371	0,545455

Table 9: sEMG correlations results. Spearman correlation was used to evaluate dependencies among agonist-antagonist pairs of muscles for every child's LIL and MIL separately pre- and post-intervention. This table shows an overview of Spearman correlation (rho-value) results. Statistically significant results (rho<0.5) are marked with yellow color. *Legend:* More impaired limb (MIL); Less impaired limb (LIL); Initial contact (IC); Loading response (LR); Midstance (MST); Terminal stance (TS); Pre-swing (PSW); Initial swing (ISW); Midswing (MSW); Terminal swing (TSW); BF (biceps femoris); RF (rectus femoris); TA (tibialis anterior); MG (medial gastrocnemius).

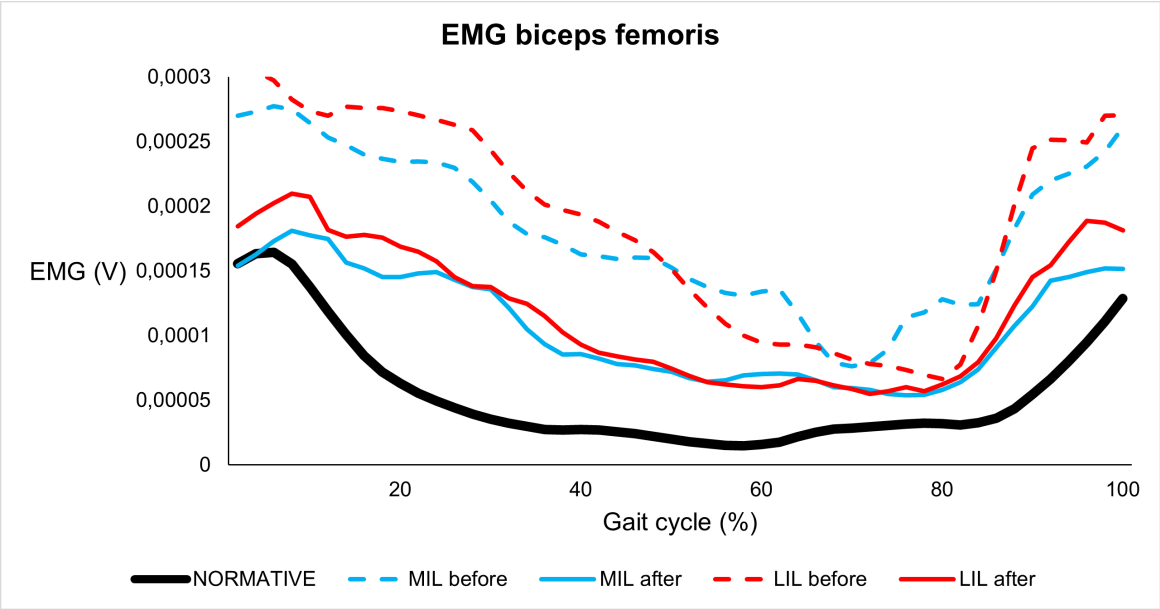

Figure 3: Qualitative pre-post intervention changes in sEMG activity of biceps femoris. The interpretation is as follows: each of the muscles was divided into MIL and LIL pre-post intervention condition that was further compared with normative data curves (Hof et al., 2005; Winter, 2009) from typically developing children ('normative'). Changes are shown through the gait cycle phases and expressed in percents (axis x); and corresponding EMG values expressed in Volts (V) (axis y). Black curve expresses normative data curves ('normative'); dotted blue curve expresses MIL pre-intervention ('MIL pre'); blue curve expresses MIL post-intervention ('MIL post'); dotted red curve expresses LIL pre-intervention ('LIL pre'); red curve expresses LIL post-intervention ('LIL post'). Biceps femoris decreased activity bilaterally and the curve of CP children tend to show a more physiological activation trend when compared to the normative curve. *Legend:* More impaired limb (MIL); Less impaired limb (LIL).

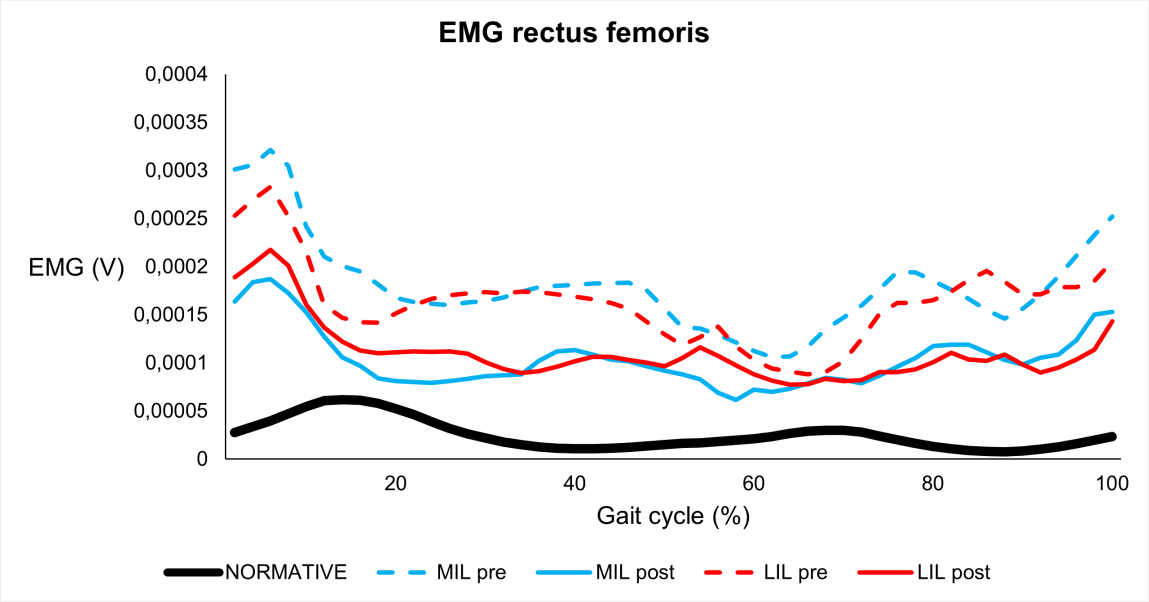

Figure 4: Qualitative pre-post intervention changes in sEMG activity of rectus femoris. The interpretation is as follows: each of the muscles was divided into MIL and LIL pre-post intervention condition that was further compared with normative data curves (Hof et al., 2005; Winter, 2009) from typically developing children ('normative'). Changes are shown through the gait cycle phases and expressed in percents (axis x); and corresponding EMG values expressed in Volts (V) (axis y). Black curve expresses normative data curves ('normative'); dotted blue curve expresses MIL pre-intervention ('MIL pre'); blue curve expresses MIL post-intervention ('MIL post'); dotted red curve expresses LIL pre-intervention ('LIL pre'); red curve expresses LIL post-intervention ('LIL post'). Rectus femoris decreased activity bilaterally almost across all gait cycle phases, however, the trend of the non-physiological curve is still present. *Legend:* More impaired limb (MIL); Less impaired limb (LIL).

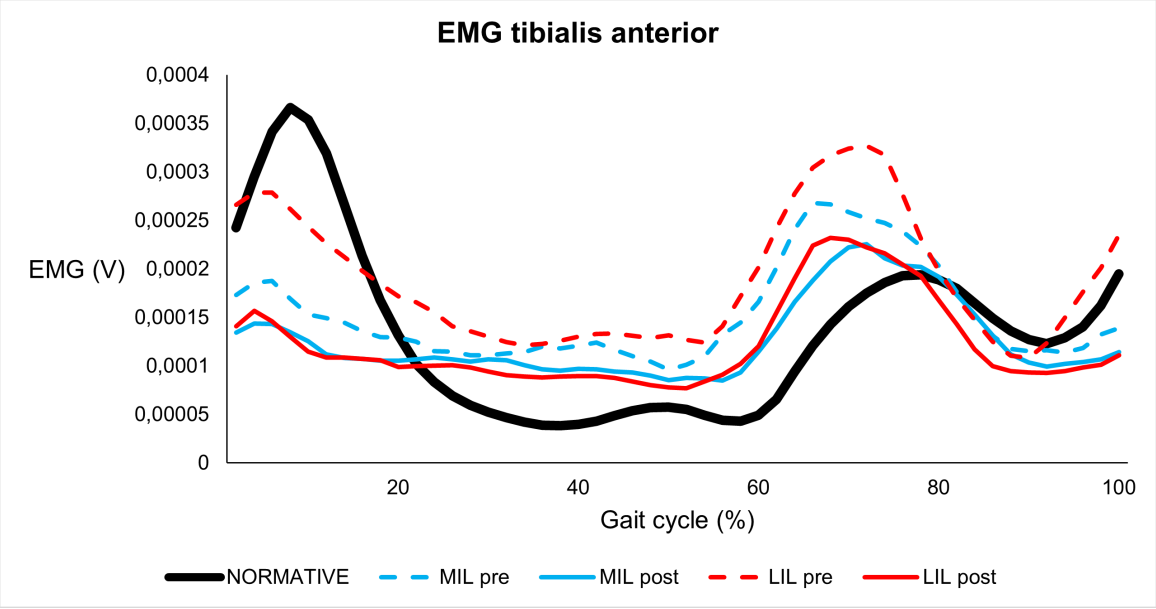

Figure 5: Qualitative pre-post intervention changes in sEMG activity of tibialis anterior. The interpretation is as follows: each of the muscles was divided into MIL and LIL pre-post intervention condition that was further compared with normative data curves (Hof et al., 2005; Winter, 2009) from typically developing children ('normative'). Changes are shown through the gait cycle phases and expressed in percents (axis x); and corresponding EMG values expressed in Volts (V) (axis y). Black curve expresses normative data curves ('normative'); dotted blue curve expresses MIL pre-intervention ('MIL pre'); blue curve expresses MIL post-intervention ('MIL post'); dotted red curve expresses LIL pre-intervention ('LIL pre'); red curve expresses LIL post-intervention ('LIL post'). Although tibialis anterior showed decreased activity almost in all phases except for terminal stance and mid-swing, the curve of CP children tends to show a more physiological activation trend when compared to the normative curve. *Legend:* More impaired limb (MIL); Less impaired limb (LIL).

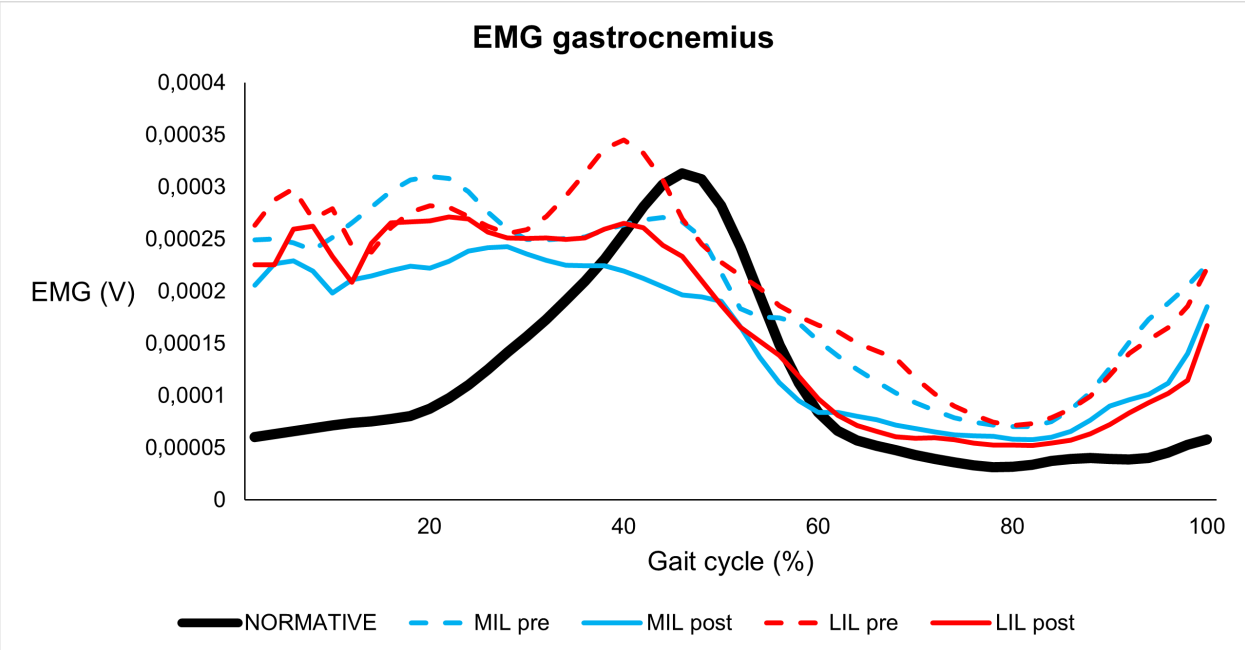

Figure 6: Qualitative pre-post intervention changes in sEMG activity of medial gastrocnemius. The interpretation is as follows: each of the muscles was divided into MIL and LIL pre-post intervention condition that was further compared with normative data curves (Hof et al., 2005; Winter, 2009) from typically developing children ('normative'). Changes are shown through the gait cycle phases expressed in percents (axis x); and corresponding EMG values expressed in Volts (V) (axis y). Black curve expresses normative data curves ('normative'); dotted blue curve expresses MIL pre-intervention ('MIL pre'); blue curve expresses MIL post-intervention ('MIL post'); dotted red curve expresses LIL pre-intervention ('LIL pre'); red curve expresses LIL post-intervention ('LIL post'). Medial gastrocnemius decreased activity mainly in terminal stance, mid-swing and terminal swing phases, the curve of CP children tends to show a more physiological activation trend when compared to the normative curve. *Legend:* More impaired limb (MIL); Less impaired limb (LIL).

3.3.2. Joint kinematics results

The most significant bilateral kinematic changes were observed in hip rotations, foot progress, and thorax tilt followed by small to moderate effect sizes ranging between -0,41633 to -0.6245 (see Table 10). Internal hip rotation decreased almost across all phases. Foot progress angles showed a decreased trend of in-toeing almost across all phases. A decrease of anterior thorax tilt was observed bilaterally, however it was more accented on the less impaired side of the trunk. Table 10 summarizes joint kinematics quantitative changes including effect sizes for all children with CP. Examples of qualitative changes in joint kinematics activity together with normative data curves from typically developing children are shown in Figures 20-23.

In general, moderate to large correlations ranging between -0.6 to 0.8286 were found. Table 11 summarizes joint kinematics pairs quantitative changes for all children with CP. Significant correlations in joint kinematics pairs in terms of their physiological range of motion were found bilaterally in pelvic tilt/knee flexion extension in pre-swing phase; knee flexion extension/ankle flexion extension in mid stance and initial swing phases; hip rotation/knee abduction adduction in midswing phase; and finally in thorax tilt/pelvic tilt across phases terminal swing up to initial swing.

Kinematics	Gait phase (p-value) / *Effect size*							
	IC	LR	MST	TS	PSW	ISW	MSW	TSW
Pelvic tilt MIL	0,346522	0,388186	0,58292	0,432768	0,388186	0,307821	0,307821	0,307821
ES	*0,192154*	*0,176141*	*0,11209*	*0,160128*	*0,176141*	*0,208167*	*0,208167*	*0,208167*
Pelvic tilt LIL	0,346522	0,346522	0,346522	0,307821	0,388186	0,530285	0,480177	0,346522
ES	*0,192154*	*0,192154*	*0,192154*	*0,208167*	*0,176141*	*0,128103*	*0,144115*	*0,192154*
Pelvic obliquity MIL	1	0,937473	0,307821	0,084379	0,028056	0,209427	0,813945	0,813945
ES	*0*	*0,016013*	*0,208167*	*0,352282*	*-0,44836*	*-0,25621*	*-0,04804*	*-0,04804*
Pelvic obliquity LIL	0,03417	0,116664	0,346522	0,937473	0,753684	0,388186	0,084379	0,03417
ES	*0,432346*	*-0,32026*	*-0,19215*	*0,016013*	*0,064051*	*0,176141*	*0,352282*	*0,432346*
Pelvic rotation MIL	0,63787	0,694887	0,272095	0,099481	0,157939	0,480177	0,813945	0,875329
ES	*-0,09608*	*-0,08006*	*-0,22418*	*0,336269*	*0,288231*	*0,144115*	*0,048038*	*0,032026*
Pelvic rotation LIL	0,071189	0,157939	0,346522	0,63787	0,937473	0,58292	0,239317	0,209427
ES	*0,368295*	*0,288231*	*0,192154*	*-0,09608*	*-0,01601*	*-0,11209*	*-0,24019*	*-0,25621*
Hip flexion/extension MIL	0,813945	0,813945	0,530285	0,63787	0,307821	0,157939	0,209427	0,432768
ES	*0,048038*	*0,048038*	*0,128103*	*0,096077*	*-0,20817*	*0,288231*	*0,256205*	*0,160128*
Hip flexion/extension LIL	0,272095	0,209427	0,099481	0,028056	0,239317	0,071189	0,071189	0,157939
ES	*0,224179*	*0,256205*	*0,336269*	*0,448359*	*-0,24019*	*0,368295*	*0,368295*	*0,288231*
Hip abduction/adduction MIL	0,136097	0,239317	0,099481	0,272095	0,157939	0,209427	0,272095	0,239317
ES	*-0,30424*	*0,240192*	*0,336269*	*0,224179*	*-0,28823*	*-0,25621*	*-0,22418*	*-0,24019*
Hip abduction/adduction LIL	0,157939	0,157939	0,480177	0,58292	0,694887	0,875329	0,875329	0,346522
ES	*0,288231*	*-0,28823*	*-0,14412*	*-0,11209*	*-0,08006*	*-0,03203*	*-0,03203*	*0,192154*
Hip rotation MIL	0,004742	0,003702	0,002218	0,002218	0,002218	0,002218	0,003702	0,00604
ES	*-0,57646*	*-0,59247*	*-0,6245*	*-0,6245*	*-0,6245*	*-0,6245*	*0,592474*	*0,560449*
Hip rotation LIL	0,157939	0,116664	0,04986	0,022909	0,041389	0,022909	0,022909	0,028056
ES	*-0,28823*	*-0,32026*	*-0,40032*	*-0,46437*	*-0,41633*	*-0,46437*	*0,464372*	*0,448359*
Knee flexion/extension MIL	0,432768	0,753684	0,346522	0,182338	0,58292	0,059739	0,239317	0,239317
ES	*-0,16013*	*-0,06405*	*-0,19215*	*-0,27222*	*-0,11209*	*-0,38431*	*-0,24019*	*-0,24019*
Knee flexion/extension LIL	0,694887	0,694887	0,694887	0,388186	0,694887	0,875329	0,813945	0,937473
ES	*0,080064*	*0,080064*	*0,080064*	*0,176141*	*0,080064*	*0,032026*	*-0,04804*	*-0,01601*
Knee abduction/adduction MIL	0,03417	0,03417	0,04986	0,099481	0,03417	0,018603	0,022909	0,018603
ES	*0,432346*	*0,432346*	*0,40032*	*0,336269*	*0,432346*	*-0,48038*	*0,464372*	*0,480384*
Knee abduction/adduction LIL	0,272095	0,272095	0,182338	0,63787	0,209427	0,059739	0,099481	0,03417
ES	*0,224179*	*0,224179*	*0,272218*	*0,096077*	*0,256205*	*-0,38431*	*0,336269*	*0,432346*
Ankle plantar/dorsal flexion MIL	0,239317	0,307821	0,480177	1	0,813945	0,157939	0,157939	0,875329
ES	*0,240192*	*0,208167*	*0,144115*	*0*	*-0,04804*	*0,288231*	*0,288231*	*0,032026*
Ankle plantar/dorsal flexion LIL	0,58292	0,480177	0,937473	0,346522	0,346522	0,530285	0,272095	0,63787
ES	*0,11209*	*0,144115*	*-0,01601*	*-0,19215*	*-0,19215*	*0,128103*	*0,224179*	*0,096077*
Foot tilt MIL	0,286003	0,373945	0,432768	0,753684	0,480177	0,813945	0,239317	0,209427
ES	*-0,21779*	*-0,18149*	*-0,16013*	*0,064051*	*0,144115*	*-0,04804*	*-0,24019*	*-0,25621*
Foot tilt LIL	0,116664	0,084379	0,059739	0,136097	0,432768	0,432768	0,813945	0,272095
ES	*0,320256*	*0,352282*	*0,384308*	*0,304243*	*0,160128*	*0,160128*	*0,048038*	*0,224179*
Foot progress MIL	0,012792	0,016369	0,00604	0,004742	0,015022	0,012063	0,028056	0,04986
ES	*-0,50817*	*-0,49002*	*-0,56045*	*-0,57646*	*-0,4964*	*-0,51241*	*-0,44836*	*-0,40032*
Foot progress LIL	0,00604	0,007649	0,022909	0,002873	0,002218	0,059739	0,116664	0,03417
ES	*-0,56045*	*-0,54444*	*-0,46437*	*-0,60849*	*-0,6245*	*-0,38431*	*-0,32026*	*-0,43235*
Thorax tilt MIS*	0,050461	0,050461	0,050461	0,022909	0,018603	0,018603	0,041389	0,03417
ES	*0,399275*	*0,399275*	*-0,39928*	*0,464372*	*-0,48038*	*-0,48038*	*-0,41633*	*-0,43235*
Thorax tilt LIS*	0,028056	0,028056	0,03417	0,03417	0,03417	0,028056	0,022909	0,028056
ES	*0,448359*	*0,448359*	*-0,43235*	*0,432346*	*-0,43235*	*-0,44836*	*-0,46437*	*-0,44836*

Table 10: Joint kinematics results. The deviation of CP signals from the normative kinematics values (Hof et al., 2005; Winter, 2009) of each variable was calculated by cross-correlation for every child's LIL and MIL separately pre- and post-intervention. Afterward, cross-correlation values 'pre-post intervention' were compared by using the Wilcoxon sign rank test. This table shows an overview of Wilcoxon sign rank test (p-value) results, including effect sizes for all variables across gait phases. Statistically significant results ($p<0.05$) are marked with yellow color. *Legend: ES* (effect size); More impaired limb (MIL); Less impaired limb (LIL); More impaired side (MIS); Less impaired side (LIS).

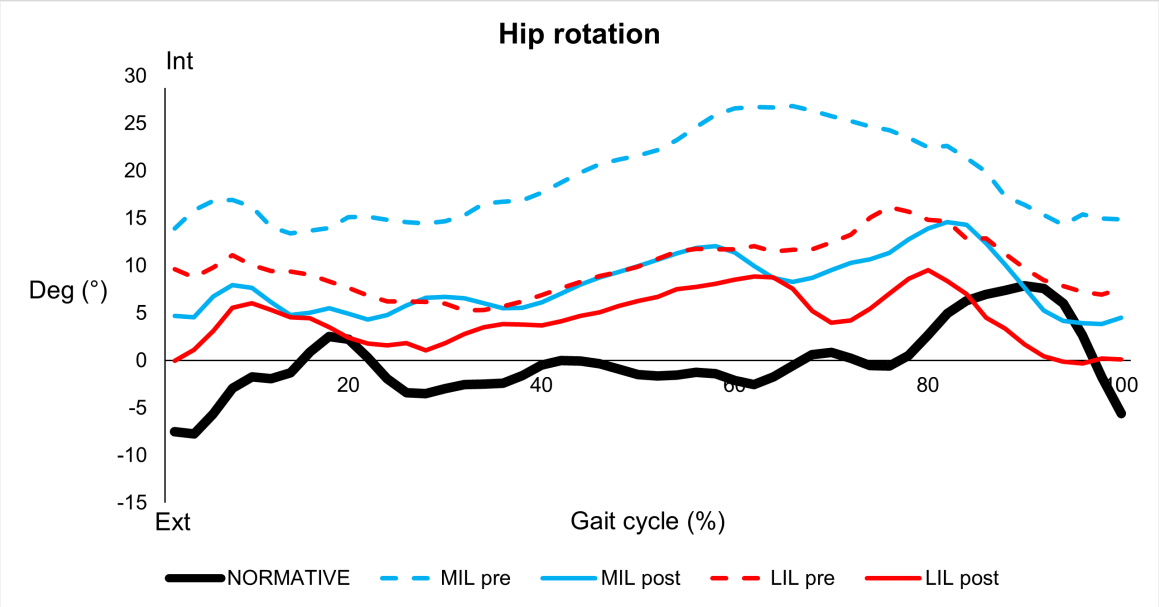

Figure 7: Qualitative pre-post intervention changes in hip rotations. The interpretation is as follows: each of the variables was divided into MIL and LIL pre-post intervention condition that was further compared with normative data curves (Hof et al., 2005; Winter, 2009) from typically developing children ('normative'). Changes are shown through the gait cycle phases and expressed in percents (axis x); and corresponding joint range of motion values expressed in degrees (°) (axis y). Black curve expresses

normative data curves ('normative'); dotted blue curve expresses MIL pre-intervention ('MIL pre'); blue curve expresses MIL post-intervention ('MIL post'); dotted red curve expresses LIL pre-intervention ('LIL pre'); red curve expresses LIL post-intervention ('LIL post'). Internal hip rotation decreased bilaterally almost across all gait cycle phases and the curve of CP children tend to show more physiological activation trend when compared to the normative curve. *Legend:* More impaired limb (MIL); Less impaired limb (LIL); Less impaired side (LIS); degree (Deg).

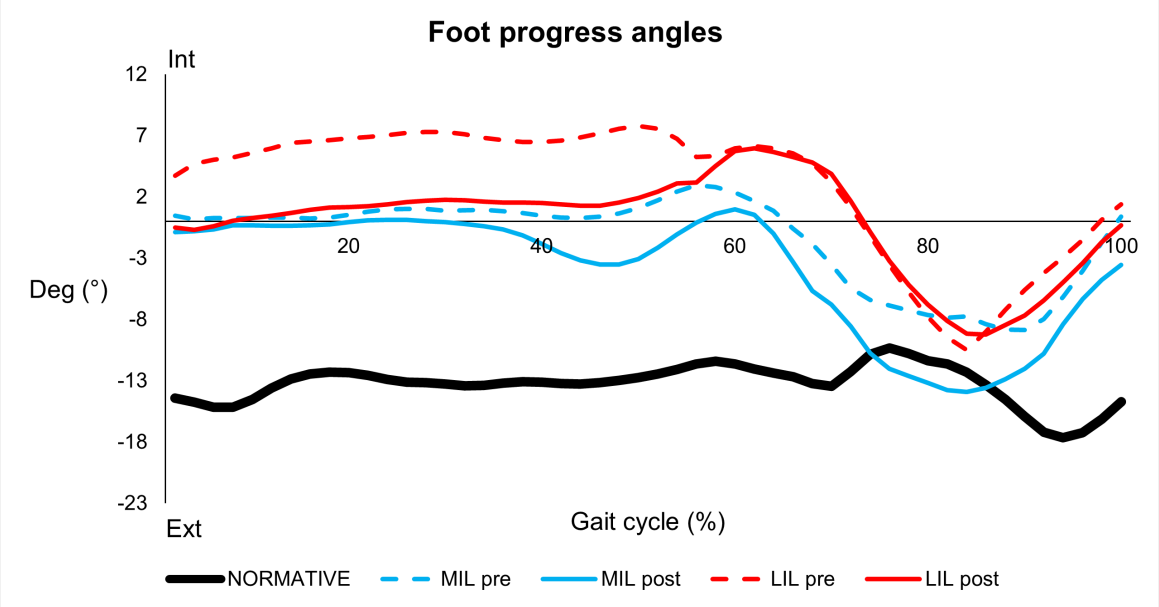

Figure 8: Qualitative pre-post intervention changes in foot progress angle. The interpretation is as follows: each of the variables was divided into MIL and LIL pre-post intervention condition that was further compared with normative data curves (Hof et al., 2005; Winter, 2009) from typically developing children (‘normative'). Changes are shown through the gait cycle phases and expressed in percents (axis x); and corresponding joint range of motion values expressed in degrees (°) (axis y). Black curve expresses normative data curves ('normative'); dotted blue curve expresses MIL pre-intervention ('MIL pre'); blue curve expresses MIL post-

intervention ('MIL post'); dotted red curve expresses LIL pre-intervention ('LIL pre'); red curve expresses LIL post-intervention ('LIL post'). Although in-toeing significantly decreased almost across all phases, the trend of the non-physiological curve is still present. *Legend:* More impaired limb (MIL); Less impaired limb (LIL); Less impaired side (LIS); degree (Deg).

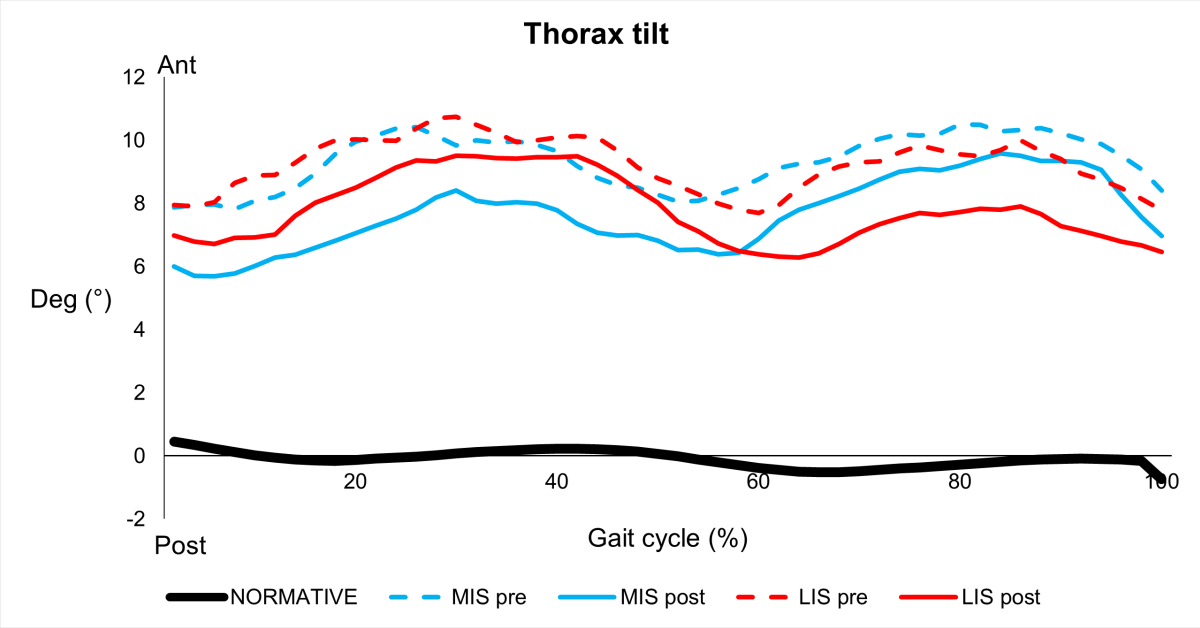

Figure 9: Qualitative pre-post intervention changes in thorax tilt. The interpretation is as follows: each of the variables was divided into MIL and LIL pre-post intervention condition that was further compared with normative data curves (Hof et al., 2005; Winter, 2009) from typically developing children ('normative'). Changes are shown through the gait cycle phases and expressed in percents (axis x); and corresponding joint range of motion values expressed in degrees (°) (axis y). Black curve expresses normative data curves ('normative'); dotted blue curve expresses MIL pre-intervention ('MIL pre'); blue curve expresses MIL post-intervention ('MIL post'); dotted red curve expresses LIL pre-intervention ('LIL pre'); red curve expresses LIL post-intervention ('LIL post'). Anterior thorax tilt showed bilateral decreasing that was even more accented on the LIS of the trunk, however, the trend of the non-

physiological curve is still present. *Legend:* More impaired limb (MIL); Less impaired limb (LIL); Less impaired side (LIS); degree (Deg).

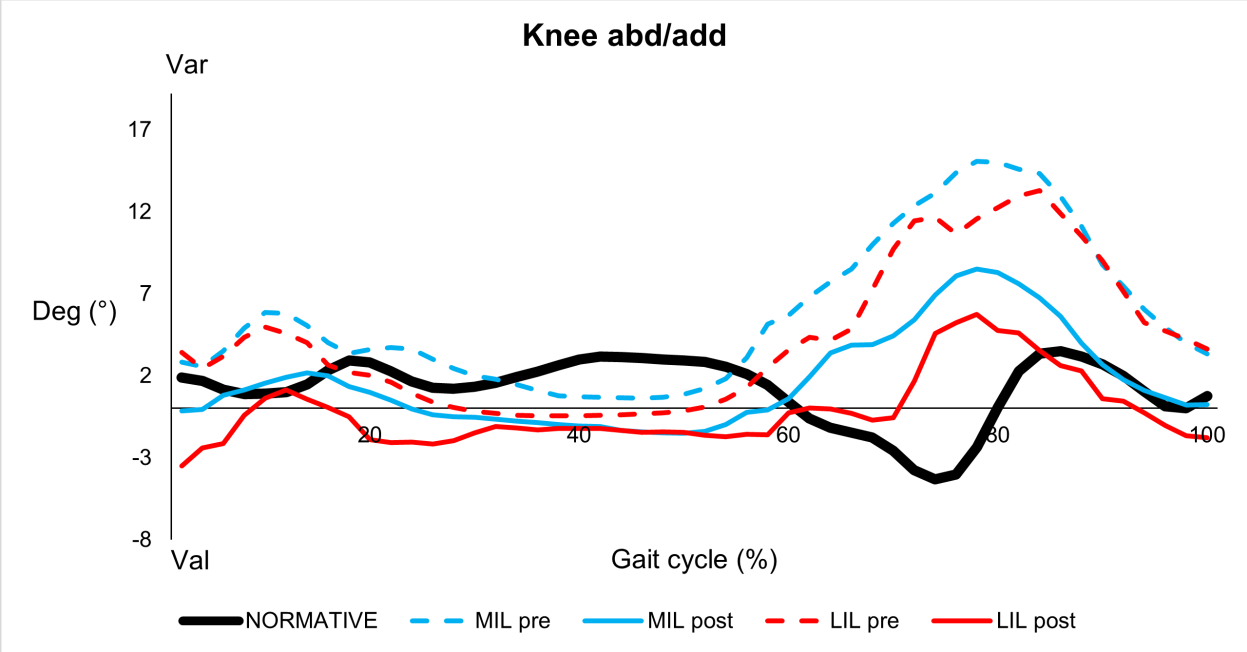

Figure 10: Qualitative pre-post intervention changes in knee abduction-adduction. The interpretation is as follows: each of the variables was divided into MIL and LIL pre-post intervention condition that was further compared with normative data curves (Hof et al., 2005; Winter, 2009) from typically developing children (‘normative’). Changes are shown through the gait cycle phases and expressed in percents (axis x); and corresponding joint range of motion values expressed in degrees (°) (axis y). Black curve expresses normative data curves ('normative'); dotted blue curve expresses MIL pre-intervention ('MIL pre'); blue curve expresses MIL post-intervention ('MIL post'); dotted red curve expresses LIL pre-intervention ('LIL pre'); red curve expresses LIL post-intervention ('LIL post'). Although knee abduction-adduction decreased mainly in swing phases, the trend of the

non-physiological curve is still present. *Legend:* More impaired limb (MIL); Less impaired limb (LIL); degree (Deg).

Kinematics/kinetics correlations	Gait phase (rho value)							
	IC	LR	MST	TS	PSW	ISW	MSW	TSW
Pelvic tilt/Knee flexion extension MIL	-0,02797	0	-0,3455	-0,3939	-0,7	0,0857	0,2381	-0,4857
Pelvic tilt/Knee flexion extension LIL	0,335664	-0,7	-0,6606	-0,8909	0,6	-0,0286	0,2381	0,3714
Hip flexion extension/Knee flexion extension MIL	0,475524	-0,3	-0,3212	-0,6667	0,4	0,0286	0,0952	0,4286
Hip flexion extension/Knee flexion extension LIL	0,251748	-0,2	0,4424	0,3455	-0,9	-0,6	0,381	0,2
Knee flexion extension/Ankle flexion extension MIL	0,116664	0	0,7818	-0,4788	-0,1	0,5429	-0,1905	0,2571
Knee flexion extension/Ankle flexion extension LIL	0,454545	-0,7	0,8182	-0,4424	-0,3	0,7143	-0,381	0,4286
Hip rotation/Knee abduction adduction MIL	0,475524	-0,1	0,503	0,0909	0,2	-0,2	0,6667	-0,0286
Hip rotation/Knee abduction adduction LIL	0,342657	-0,1	0,0424	-0,0667	-0,1	-0,2	0,7857	-0,1429
Hip abduction adduction/Knee abduction adduction MIL	-0,02797	0,9	-0,0788	0,3212	-0,6	-0,2571	-0,4524	0,6571
Hip abduction adduction/Knee abduction adduction LIL	-0,2571	-0,3	-0,2485	-0,3091	0,3	0,1429	-0,6905	0,2571
Thorax tilt//Pelvic tilt MIL	0,0857	-0,3	0,3455	0,5636	0,9	0,8286	-0,22143	0,7714
Thorax tilt//Pelvic tilt LIL	0,0286	0,1	0,3333	0,7333	-0,6	0,6	0,6905	0,3143

Table 11: Joint kinematics/kinetics correlations results. Spearman correlation was used to evaluate dependencies among kinematic variables for every child's LIL and MIL separately pre- and post-intervention. This table shows an overview of Spearman correlation (rho-value) results. Statistically significant results (rho<0.5) are marked with yellow color. *Legend:* More impaired limb (MIL); Less impaired limb (LIL); Initial contact (IC); Loading response (LR); Midstance (MST); Terminal stance (TS); Pre-swing (PSW); Initial swing (ISW); Midswing (MSW); Terminal swing (TSW).

3.3.3. Kinetics results

Kinetics showed a very few significant changes that were observed unilaterally and in a single gait phase only. These findings are further supported by small effect sizes ranging between -0,528342 to 0,41633 (see Table 12). Table 12 summarizes kinetics quantitative changes including effect sizes for all children with CP.

Kinetics	Gait phase (p-value) / *Effect size*							
	IC	LR	MST	TS	PSW	ISW	MSW	TSW
Hip flexion/extension moment MIL	0,480177	0,022909	0,084379	0,530285	0,63787	0,346522	0,157939	0,789675
ES	*-0,14412*	*-0,46437*	*-0,35228*	*-0,1281*	*0,096077*	*0,192154*	*-0,28823*	*-0,05445*
Hip flexion/extension moment LIL	0,346522	0,136097	0,813945	0,875329	0,432768	0,63787	0,018603	0,929153
ES	*0,192154*	*-0,30424*	*0,048038*	*0,032026*	*-0,16013*	*-0,09608*	*0,480384*	*0,018149*
Hip abduction/adduction moment MIL	0,272095	0,388186	0,937473	0,813945	1	1	0,694887	0,722108
ES	*0,224179*	*-0,17614*	*-0,01601*	*-0,04804*	*0*	*0*	*-0,08006*	*-0,0726*
Hip abduction/adduction moment LIL	0,182338	0,480177	0,63787	0,63787	0,58292	0,753684	0,307821	1
ES	*0,272218*	*-0,14412*	*-0,09608*	*-0,09608*	*0,11209*	*-0,06405*	*-0,20817*	*0*
Hip power MIL	0,937473	0,432768	0,694887	0,694887	0,260393	0,284503	0,937473	0,071189
ES	*-0,01601*	*0,160128*	*-0,08006*	*0,080064*	*0,229734*	*0,218466*	*0,016013*	*0,368295*
Hip power LIL	0,059739	0,247746	0,136097	0,239317	0,130665	0,575062	0,656642	0,209427
ES	*0,384308*	*0,235935*	*0,304243*	*-0,24019*	*-0,30853*	*-0,11443*	*0,090744*	*0,256205*
Knee flexion/extension moment MIL	0,012063	0,388186	0,307821	0,084379	0,58292	0,63787	0,813945	0,084379
ES	*-0,51241*	*-0,17614*	*-0,20817*	*0,352282*	*-0,11209*	*-0,09608*	*0,048038*	*-0,35228*
Knee flexion/extension moment LIL	0,157939	0,009633	0,059739	0,116664	0,209427	0,307821	0,63787	0,694887
ES	*-0,28823*	*-0,52842*	*-0,38431*	*0,320256*	*-0,25621*	*-0,20817*	*0,096077*	*-0,08006*
Knee valgus/varus moment MIL	0,753684	0,307821	0,059739	0,753684	0,530285	0,041389	0,530285	0,239317
ES	*0,064051*	*-0,20817*	*-0,38431*	*0,064051*	*-0,1281*	*0,416333*	*0,128103*	*0,240192*
Knee valgus/varus moment LIL	0,071189	0,937473	0,875329	0,875329	0,346522	0,480177	0,099481	0,272095
ES	*-0,3683*	*-0,01601*	*-0,03203*	*0,032026*	*0,192154*	*-0,14412*	*-0,33627*	*-0,22418*
Knee power MIL	0,432768	0,480177	0,753684	0,480177	0,51467	0,284503	0,813945	0,209427
ES	*-0,16013*	*0,144115*	*0,064051*	*-0,14412*	*-0,133*	*-0,21847*	*0,048038*	*0,256205*
Knee power LIL	0,937473	0,789675	0,480177	0,157939	0,15486	0,074462	0,929153	0,480177
ES	*-0,01601*	*-0,05445*	*-0,14412*	*-0,28823*	*0,290382*	*0,36411*	*0,018149*	*-0,14412*
Ankle flexion/extension moment MIL	0,694887	0,813945	0,530285	0,307821	0,432768	0,182338	0,307821	0,157939
ES	*-0,08006*	*0,048038*	*-0,1281*	*-0,20817*	*0,160128*	*0,272218*	*-0,20817*	*-0,28823*
Ankle flexion/extension moment LIL	0,63787	0,182338	0,937473	0,209427	0,875329	0,58292	0,63787	0,346522
ES	*0,096077*	*0,272218*	*-0,01601*	*-0,25621*	*0,032026*	*0,11209*	*0,096077*	*-0,19215*
Ankle power MIL	0,753684	0,041389	0,530285	0,388186	0,858955	0,507624	0,480177	0,63787
ES	*-0,06405*	*-0,41633*	*-0,1281*	*-0,17614*	*-0,03627*	*-0,13524*	*-0,14412*	*-0,09608*
Ankle power LIL	0,272095	0,929153	0,530285	0,694887	0,020795	0,444587	0,476907	0,813945
ES	*0,224179*	*-0,01815*	*0,128103*	*-0,08006*	*-0,47187*	*0,156047*	*-0,14519*	*0,048038*
GRF X MIL	0,656642	0,130665	0,432768	0,136097	0,161429			
ES	*-0,09074*	*-0,30853*	*-0,16013*	*-0,30424*	*-0,28583*			
GRF X LIL	1	0,109511	0,157939	0,239317	0,209427			
ES	*0*	*-0,32668*	*-0,28823*	*-0,24019*	*-0,25621*			
GRF Y MIL	0,423596	0,423596	0,239317	0,272095	0,400814			
ES	*-0,16334*	*-0,16334*	*0,240192*	*0,224179*	*0,171499*			
GRF Y LIL	0,858863	0,476907	0,753684	0,480177	0,875329			
ES	*-0,0363*	*0,145191*	*0,064051*	*-0,14412*	*-0,03203*			
GRF Z MIL	0,480177	0,530285	0,937473	0,530285	0,575403			
ES	*0,144115*	*0,128103*	*-0,01601*	*0,128103*	*0,114332*			
GRF Z LIL	0,789675	0,247746	0,388186	0,937473	0,015022			
ES	*0,054447*	*0,235935*	*0,176141*	*-0,01601*	*-0,4964*			
COM MIL	0,789675	0,929153	0,239317	0,63787	0,875329	0,875329	0,346522	0,239317
ES	*0,054447*	*0,018149*	*0,240192*	*0,096077*	*0,032026*	*-0,03203*	*0,192154*	*-0,24019*
COM LIL	0,432768	0,480177	0,694887	0,753684	1	0,937473	0,136097	0,480177
ES	*0,160128*	*0,144115*	*0,080064*	*0,064051*	*0*	*0,016013*	*0,304243*	*-0,14412*
COP X MIL	0,530285	0,875329	1	0,239317	0,865772			
ES	*0,128103*	*-0,03203*	*0*	*-0,24019*	*-0,0345*			
COP X LIL	0,858863	0,878482	0,813945	0,937473	0,888638			
ES	*0,036298*	*0,031209*	*0,048038*	*0,016013*	*-0,02858*			
COP Y MIL	0,116664	0,059739	0,136097	0,272095	0,236724			
ES	*-0,32026*	*-0,38431*	*-0,30424*	*-0,22418*	*-0,24152*			
COP Y LIL	0,373945	0,575062	0,136097	0,272095	0,207578			
ES	*0,181489*	*-0,11443*	*-0,30424*	*-0,22418*	*-0,25725*			

Table 12: Kinetics results. The deviation of CP signals from the normative kinetics values (Hof et al., 2005; Winter, 2009) from typically developing children ('normative') of each variable was calculated by cross-correlation for every child's LIL and MIL separately pre- and post-intervention. Afterward, cross-correlation values "pre-post intervention" were compared by using the Wilcoxon sign rank test. This table shows an overview of Wilcoxon sign rank test (p-value) results, including effect sizes for all variables across gait phases. Statistically significant results ($p<0.05$) are marked with yellow color. *Legend:* ES (effect size); More impaired limb (MIL); Less impaired limb (LIL); Initial contact (IC); Loading response (LR); Midstance (MST); Terminal stance (TS); Pre-swing (PSW); Initial swing (ISW); Midswing (MSW); Terminal swing (TSW).

3.3.4. Spatiotemporal parameters results

Generally, statistically significant differences were found in the vast majority of spatiotemporal parameters followed by moderate effect sizes (see Table 13). The most important changes were increased cadence; step length; step width and walking speed. On the other, there was significant decrease in time needed for double support; stride length and stride time. Table 13 summarizes spatiotemporal parameters quantitative changes including effect sizes for all children with CP. Furthermore, median values changes for variables that showed statistically significant differences are shown in Table 14.

Spatiotemporal parameters	Pre-post condition (p-value) / *Effect size*
Cadence MIL	0,0025
ES	*0,569871*
Cadence LIL	0,0038
ES	*0,592474*
Double support MIL	0,0004
ES	*0,40032*
Double support LIL	0,0004
ES	*0,448359*
Foot off MIL	0,0385
ES	*0,6245*
Foot off LIL	0,0063
ES	*0,592474*
Opposite foot contact MIL	0,1459
ES	*0,116664*
Opposite foot contact LIL	0,3876
ES	*-0,288231*
Opposite foot off MIL	0,3876
ES	*-0,288231*
Opposite foot off LIL	1,2255
ES	*0,116664*
Single support MIL	0,3876
ES	*0,016013*
Single support LIL	1,2255
ES	*-0,034503*
Step length MIL	0,0071
ES	*0,6245*
Step length LIL	0,0064
ES	*0,560449*
Step time MIL	0,04
ES	*0,592474*
Step time LIL	0,3876
ES	*0,116664*
Step width MIL	0,0366
ES	*0,560449*
Step width LIL	0,0274
ES	*0,448359*
Stride length MIL	0,0148
ES	*0,592474*
Stride length LIL	0,0312
ES	*0,464372*
Stride time MIL	0,0071
ES	*0,576461*
Stride time LIL	0,0064
ES	*0,51241*
Walking speed MIL	0,03548
ES	*0,598912*
Walking speed LIL	0,03267
ES	*0,608487*

Table 13: Spatiotemporal parameters results. Pre-post RAGT intervention spatiotemporal median values were compared by using the Wilcoxon sign rank test. It was calculated for every child's LIL and MIL separately. This table shows an overview of Wilcoxon sign rank test (p-value) results, including effect sizes for all variables. Statistically significant results ($p<0.05$) are marked with yellow color. *Legend:* ES (effect size); More impaired limb (MIL); Less impaired limb (LIL).

Spatiotemporal parameters	LIL median before	LIL median after	MIL median before	MIL median after
Cadence (steps/min)	109,558	112,450	109,042	111,575
Double support (s)	0,3725	0,3392	0,3692	0,3442
Foot off (%)	65,04	64,98	64,35	64,19
Opposite foot contact (%)	51,68	51,18	48,48	48,92
Opposite foot off (%)	16,67	15,08	13,88	13,60
Single support (s)	0,3967	0,3958	0,3917	0,3908
Step length (m)	0,4367	0,4567	0,4383	0,4642
Step time (s)	0,5542	0,5475	0,6033	0,5833
Step width (m)	0,1194	0,1247	0,1198	0,1213
Stride length (m)	0,8742	0,8367	0,8733	0,8508
Stride time (s)	1,16	1,13	1,17	1,14
Walking speed (m/s)	0,811	0,863	0,801	0,875

Table 14: Median values of spatiotemporal parameters results. Pre-post RAGT intervention spatiotemporal median values were compared by using the Wilcoxon sign rank test. *Legend:* More impaired limb (MIL); Less impaired limb (LIL).

3.4. Clinical tests results

Statistically significant ($p<0.05$) pre-post RAGT intervention differences that indicate decreased joint contractures, increased selective motor control of lower extremities, and ability to walk farther distances were found.

3.4.1. Passive range of motion results

The most significant bilateral PROM changes were observed in hip and ankle joints followed by moderate effect sizes ranging between 0.432346 to 0.544436 (see Table 15). Generally, pathological contractures that were present in both joints pre-intervention decreased at least by 10°. Table 15 summarizes PROM quantitative changes including effect sizes for all children with CP. Examples of qualitative changes in PROM together with normative data from typically developing children are shown in Figure 11.

PROM	Pre-post condition (p-value) / *Effect size*
Hip extension MIL	increased by 10°(p=0.004)
ES	*0,544436*
Hip extension LIL	increased by 10°(p=0.004)
ES	*0,544436*
Hip internal rotation MIL	increased by 15°(p=0.002)
ES	*0,608487*
Hip internal rotation LIL	increased by 10°(p=0.002)
ES	*0,51241*
Hip external rotation MIL	increased by 5°(p=0.008)
ES	*0,528423*
Hip external rotation LIL	increased by 2.5°(p=0.043)
ES	*0,432346*
Knee popliteal angle unilateral MIL	increased by 5°(p=0.008)
ES	*0,528423*
Knee popliteal angle unilateral LIL	condition unchanged (p=0.246)
ES	*0,208167*
Knee popliteal angle bilateral MIL	increased by 5°(p=0.008)
ES	*0,528423*
Knee popliteal angle biilateral LIL	increased by 2.5°(p=0.043)
ES	*0,432346*
Knee extension LIL	decreased by 5°(p=0.035)
ES	*0,528423*
Knee extension MIL	decreased by 5°(p=0.004)
ES	*0,528423*
Ankle dorsiflexion with knee flexed MIL	increased by 10°(p=0.006)
ES	*0,544436*
Ankle dorsiflexion with knee flexed LIL	increased by 10°(p=0.006)
ES	*0,544436*
Ankle dorsiflexion with knee extended MIL	increased by 10°(p=0.006)
ES	*0,544436*
Ankle dorsiflexion with knee extended LIL	increased by 10°(p=0.006)
ES	*0,544436*

Table 15: PROM results. Pre-post RAGT intervention PROM values were compared by using the Wilcoxon sign rank test. It was calculated for every child's LIL and MIL separately. This table shows an overview of Wilcoxon sign rank test (p-value) results, including effect sizes for all variables. Statistically significant results ($p<0.05$) are marked with yellow color. *Legend:* ES (effect size); More impaired limb (MIL); Less impaired limb (LIL).

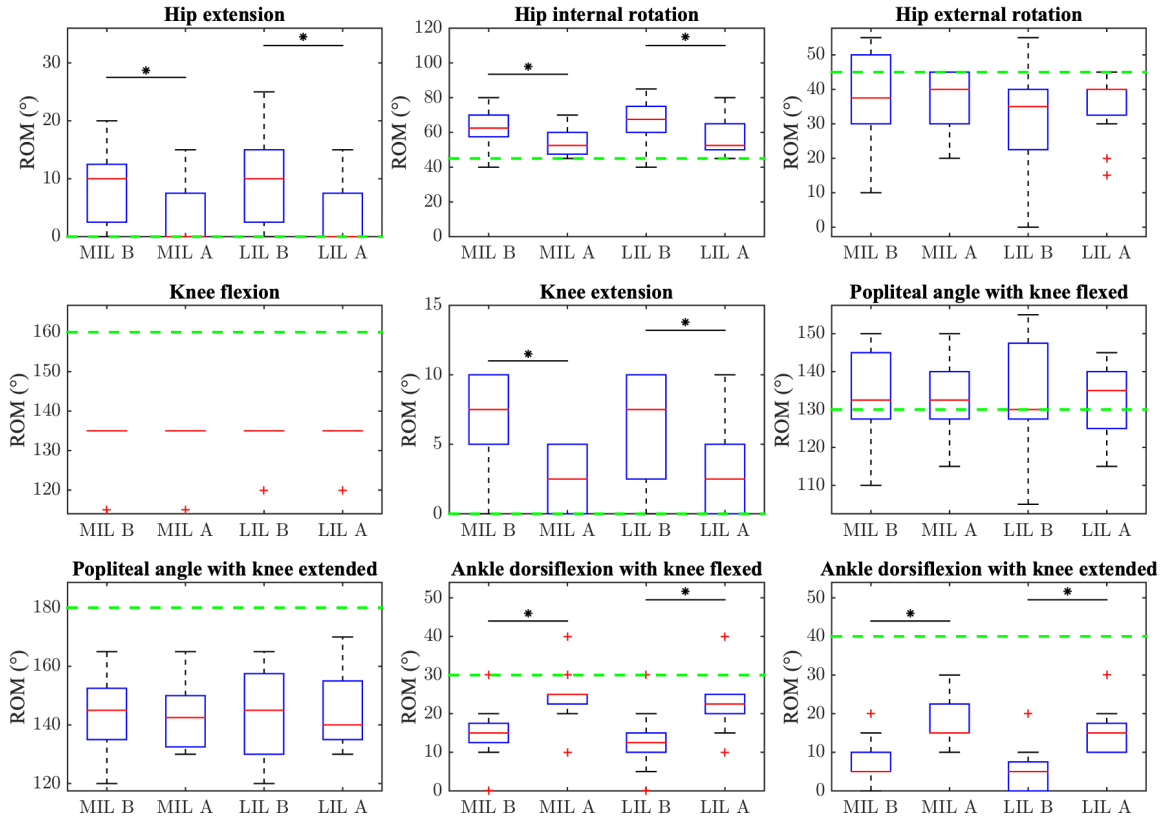

Figure 11: Qualitative pre-post intervention changes in PROM. The interpretation is as follows: box-plots represent the median values of all twelve children with CP for both MIL and LIL, pre and post-RAGT intervention (axis x). The green dotted line represents normative data (Katz et al., 1992) from typically developing children corresponding to the joint range of motion values expressed in degrees (°) (axis y). Statistically significant changes in the median values are marked with black *. *Legend:* Range of motion (ROM); More impaired limb before (MIL B); More impaired limb after (MIL A); Less impaired limb before (LIL B); Less impaired limb after (LIL A).

3.4.2. SCALE results

Total SCALE scores increased bilaterally and these findings were followed by moderate and small effect sizes ranging between 0.464372 to 0.592474 (see Table 16). Table 16 summarizes SCALE scores quantitative changes including effect sizes for all children with CP. Examples of qualitative changes in SCALE together with normative data from typically developing children are shown in Figure 12.

SCALE	Pre-post condition (p-value) / *Effect size*
Total score MIL	increased by 1.5 points (p=0.001)
ES	*0,464372*
Total score LIL	increased by 2.5 points (p=0.001)
ES	*0,592474*

Table 16: SCALE results. Pre-post SCALE scores values were compared by using the Wilcoxon sign rank test. It was calculated for every child's LIL and MIL separately. This table shows an overview of Wilcoxon sign rank test (p-value) results including effect sizes. Statistically significant results ($p<0.05$) are marked with yellow color. *Legend:* ES (effect size); More impaired limb (MIL); Less impaired limb (LIL).

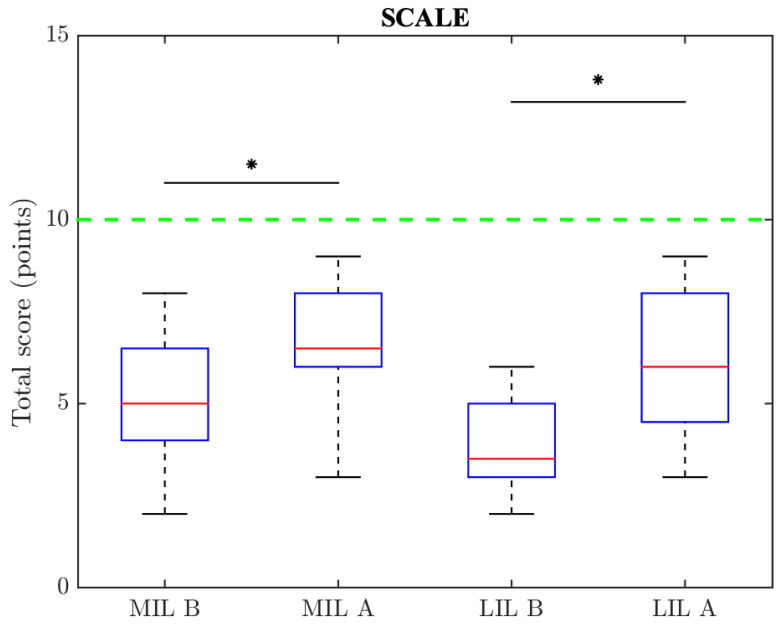

Figure 12: Qualitative pre-post intervention changes in SCALE scores. The interpretation is as follows: box-plots represent the median values of all twelve children with CP for both MIL and LIL, pre and post-RAGT intervention (axis x). The green dotted line represents normative data (Fowler, 2009) from typically developing children corresponding to the physiological SVMC expressed in points (axis y). Statistically significant changes in the median values are marked with black *. *Legend:* Selective Control Assessment of Lower Extremities (SCALE); More impaired limb before (MIL B); More impaired limb after (MIL A); Less impaired limb before (LIL B); Less impaired limb after (LIL A).

3.4.3. Six-minute walk test results

The 6MWT walking distance increased by 75 meters and this finding was followed by a strong effect size 0.6245 (see Table 17). According to Ulrich et al. (2013), the normative average distance of typically developing children is 618±79 meters. Table 17 summarizes SCALE scores quantitative changes including effect sizes for all children with CP. Examples of qualitative changes in SCALE together with normative data from typically developing children are shown in Figure 13.

6MWT	**Pre-post condition (p-value)** / *Effect size*
Total distance walked	increased by 75 meters (p=0.001)
ES	*0,6245*

Table 17: 6MWT results. Pre-post 6MWT total distance walked values were compared by using the Wilcoxon sign rank test. This table shows an overview of Wilcoxon sign rank test (p-value) results including effect size. Statistically significant results ($p<0.05$) are marked with yellow color. *Legend:* ES (effect size); 6-minute walk test (6MWT).

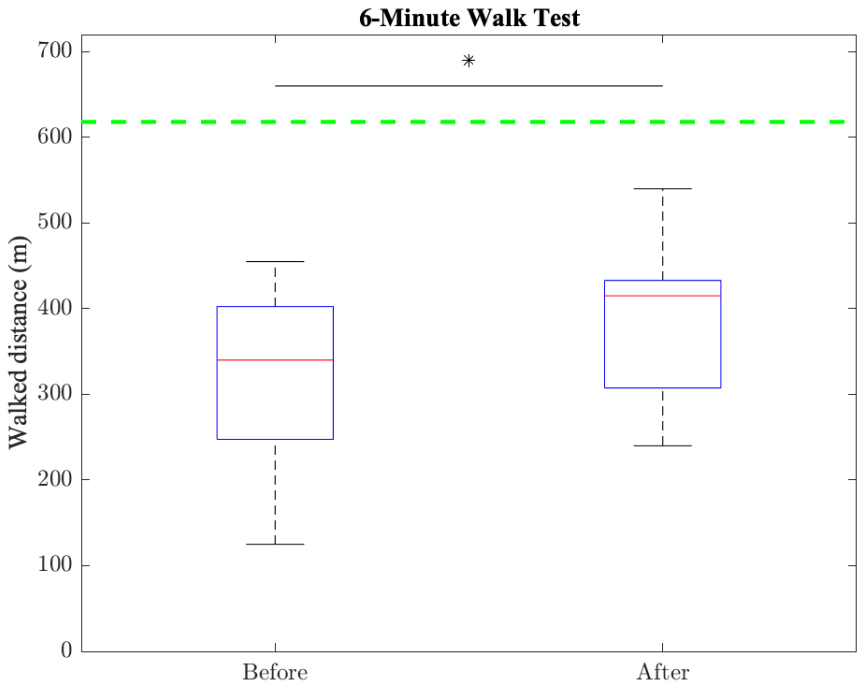

Figure 13: Qualitative pre-post intervention changes in 6MWT. The interpretation is as follows: box-plots represent the median values of all twelve children with CP for pre and post-RAGT intervention (axis x). The green dotted line represents normative data (Ulrich et al., 2013) from typically developing children expressed in meters (axis y). Statistically significant changes in the median values are marked with black *.

4. DISCUSSION

4.1. Research goals

This research study investigated whether RAGT can contribute to the improved quality of gait patterns in children with CP. The research study aimed to objectivize the effects that followed RAGT by a set of standardized, valid, and reliable methods such as CGA and clinical tests (PROM, SCALE, 6MWT).

4.2. The key findings of the research study

The key findings of the research study suggest that RAGT as monotherapy can induce more physiological muscle activity and joint kinematics trajectories, more economic energy expenditure in spatiotemporal gait parameters, increased SVMC, walking farther distances, and decreased joint contractures in CP children with spastic diparesis. Individual findings of variables are discussed below. Despite statistically significant changes, only with a deeper analysis of the gait cycle profiles and clinical tests, the results of the research study could be understood comprehensively. For that, it is strongly suggested to observe and compare changes in CGA and clinical test variables when considering any further directions of treatment/surgical management and clinical decision-making. Based on the findings, the H0: '*Gait pattern of children with CP will remain unchanged following RAGT intervention'* was rejected.

4.3. Interpretation of CGA results

4.3.1. Interpretation of sEMG results

The following chapter provides a discussion on confirmed *H1: 'RAGT will induce a more physiological sEMG muscle activity by the means of approximation to the normative curve'.*

As this study enrolled CP children with spastic diparesis, the significant improvement was found mainly in bilaterally decreased muscle activity which tends to show a more physiological activation trend when compared to the normative curve (Hof et al., 2005; Winter, 2009). Since active training seems to be more effective than passive training for motor learning and cortical reorganization in central motor impairments, RAGT likely improved muscle activation of children with CP due to active training performed with a high-repetition rate of guided movements (Meyer-Heim et al., 2009; Aurich-Schuler, 2017). Although this research study did not explore spasticity in children with CP, it could be one of the supportive explanations why RAGT led to the decrease of muscle activity. Cyclic motion has been reported to be effective in decreasing spasticity in stroke patients (Monaghan, 2017). Moderate to strong correlations were found bilaterally among agonist-antagonist pairs in terms of their more physiological activation but only in terminal swing and midswing. In the vast majority of other gait phases, correlations were observed mainly in the MIL. One of the possible explanations is that RAGT potentiated the use of MIL that generally has worsened SVMC as has been also shown in the SCALE scores. It could be explained through the stimulation of the side that appear more silent such as in hemiplegic patients. Apart from previously explained reasons that led to more physiological muscle activation, BWS is one of the directly linked parameters to

muscle activity during RAGT, and therefore should be carefully indicated to avoid pathologic couple movements in lower limbs. Bonikowski and Mrozek (2012) explored the effects of BWS in 10 children with CP that underwent RAGT with and without 30% BWS. The sEMG of RF and semitendinosus muscles was recorded 15 minutes post-training. A significant increase in EMG activity was observed in the group without BWS. These results indicate the importance of loading the patient to enhance muscle activity. In this research study, the BWS typically started with 50% unloading and was gradually decreased to 30% of children's body weight. Considering the positive effects noted in the present study combined with previous results showing that less BWS yields greater sEMG improvement. Future studies should investigate longer-duration RAGT protocols whereby the amount of BWS can be continually reduced over time, which would hypothetically improve muscle activation and coordination to an even greater extent.

4.3.2. Interpretation of joint kinematics results

The following chapter provides discussion on H2: *'RAGT will induce more physiological joint kinematics trajectories by the means of approximation to the normative curve'.* This hypothesis was confirmed only for variables hip rotation; foot progress angle; thorax tilt and knee abduction-adduction.

Generally, there is a lack of studies that explored the effect of RAGT on joint kinematics in children with CP. However, the interpretation of existing research is rather controversial due to various factors such as heterogeneity of GMFCS, or monotherapy approach versus a combination of RAGT with conventional physiotherapy. For example, Beretta et al. (2015) and (2020) suggested that combined programs of RAGT and conventional physiotherapy induce improvements

in functional activities and gait patterns in children and adolescents with acquired brain injury. This study also reported a statistically significant increase in hip extension during the terminal stance and swing phase. However, it should be highlighted that this study combined RAGT with conventional physiotherapy. A recent study conducted by Cherni et al. (2020) that enrolled 24 children with CP (GMFCS II-IV) concluded no significant changes in kinematic patterns. These results might be influenced by a wide spectrum of GMFCS groups, as well as group IV typically embraces the most severe cases of CP and children who cannot ambulate. Druzbicki et al. (2013) concluded from a controlled study on fifty-two CP children with spastic diplegia (GMFCS II-III) statistically insignificant changes among groups following Lokomat + physiotherapy, and physiotherapy only. However, a significant improvement in the maximal range of hip joint flexion ($p=0.0065$) was found. One of the used explanations was the patient's passivity during the RAGT sessions. Wallard et al. (2014) highlighted a significant improvement in knee and ankle sagittal kinematics as well as dynamic balance control following RAGT combined with virtual reality in CP children who walk in jump gait pattern after the same RAGT TP as was used in the present study. To the best of the PI's knowledge, this is the first study reporting on changes that followed RAGT in hip rotations, foot progress angles, and thorax tilt. It is assumed that RAGT likely improved the joint kinematics due to a high repetition rate of guided movements in the most neutral position and joint centered position of the pelvis and lower limbs (Kolář, 2002; Žarković and Šorfová, 2017).

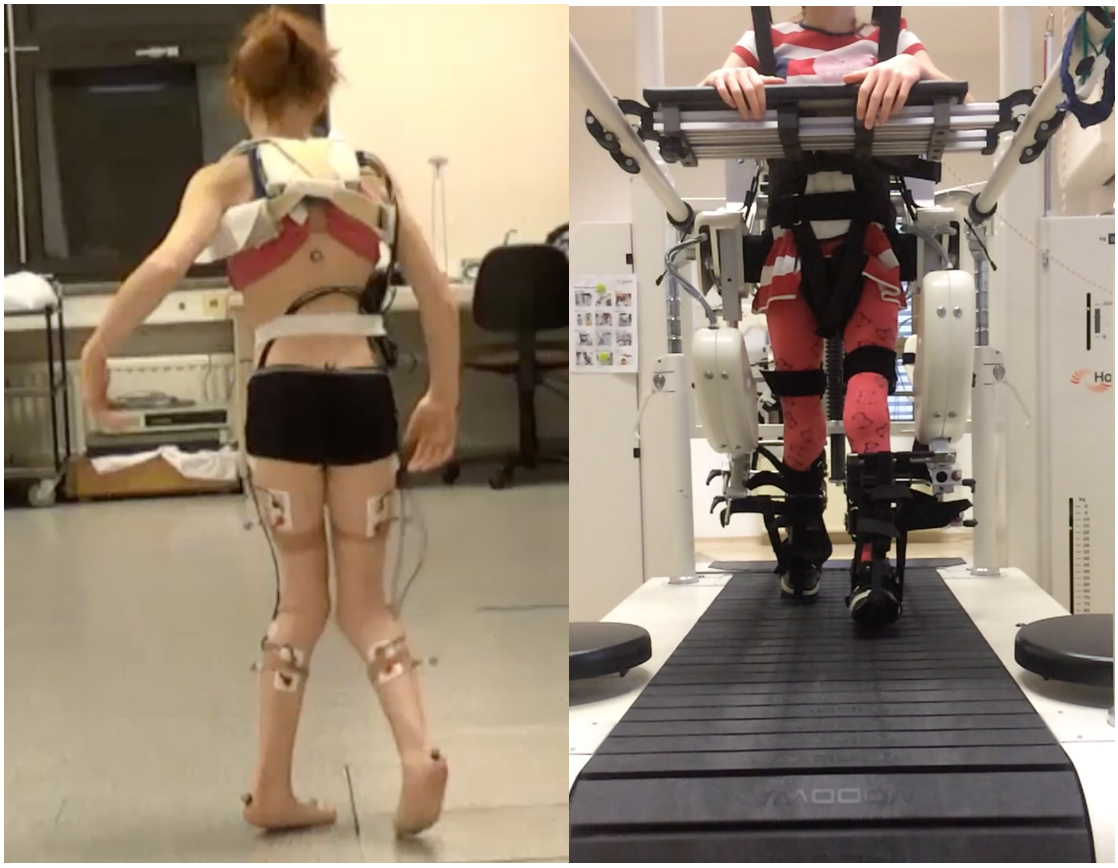

Figure 14: An 11-year-old girl with spastic diparesis ambulating in crouch gait pattern with dominantly spastic hip adductors (left). The same girl during RAGT ambulating in neutral and joint centered position of lower extremities and with extended posture (source: own).

4.3.3. Interpretation of kinetics results

The following chapter provides a discussion on rejected H3: *'RAGT will induce a more physiological gait kinetics by the means of approximation to the normative curve'.*

Joint kinetics is a component of CGA gait analysis and should be interpreted with all other information such as joint kinematics, sEMG, spatiotemporal variables, and pertinent clinical tests such as PROM. Joint kinetics provides an opportunity to understand better the role of the trunk and inter-joint relationship during gait (Perry,

2010; Armand et al., 2016). For example, the evaluation of the relationship of power generation among involved versus the non-involved side of hemiplegia patients suggests that the non-involved limb shows greater than normal power generation to compensate for the weaker non-involved limb. In general, when using joint kinetics, emphasis should be made on the pattern and timing of the specific curve in comparison to normative with less emphasis on the amplitudes of the individual peaks as suggested by Davis et al. (1991). This research study reported no quantitative nor qualitative improvements in kinetics variables that would be clinically relevant for children with CP. Furthermore, the vast majority of kinetic variables remained unchanged pre-post intervention which only suggests that RAGT has no or very low impact on kinetic variables with persistent dominance of the handicap. As there is a lack of studies that explored the effect of RAGT on kinetics in children with CP, the findings of this research study cannot be generalized but rather considered a suggestion. The PI leaves space for improvement and exploration in a greater clinical trial.

4.3.4. Interpretation of spatiotemporal parameters

The following chapter provides discussion on confirmed H4: *'RAGT will enhance the ability of children with CP to walk farther distances'.*

Definition of spatiotemporal parameters allows for an objective definition of where, when, how long, and how rapidly the individual is in contact with the ground (Perry, 2010; Baker, 2013; Armand et al., 2016). In this research study, the most important changes were observed in increased cadence; step length; step width, and walking speed. On the other, there was a significant decrease in time needed for double

support; stride length and stride time. The combination of increased cadence and walking speed together with decreased stride length and time reflects that children with CP take a high number of smaller steps, they walk faster and in a shorter period. This could potentially contribute to more economic energy expenditure, especially if ambulatory children with CP need to walk farther distances. Similar findings were reported by Beretta et al. (2015). Improved spatiotemporal parameters are also supported by the ability to walk farther distances as has been shown in the results of 6MWT.

4.4. Interpretation of clinical tests

Clinical tests are an integral part of comprehensive evaluation in children with CP. This research study aimed to choose such evaluation methods that are valid, standardized, and reliable. Apart from PROM and walk test which capture the quantitative effect of RAGT, the PI emphasized the evaluation of SVMC which has great clinical importance on SVMC, yet it is not routinely assessed. To the best of the PI's knowledge, this is the first study suggesting that RAGT improves SVMC in children with CP.

4.4.1. Interpretation of passive range of motion results

The following chapter provides a discussion on confirmed H5: *'Children with CP will increase the PROM in all joints following RAGT intervention'.*

It is common to observe a decreased PROM following a neurological injury. The PROM is assessed to determine the mobility of a joint regardless of the voluntary ability of the patient and it is usually slightly greater than active ROM and much greater in case of muscle weakness. The most important results were increased hip

extension and ankle dorsiflexion together with decreased internal hip joint rotation. RAGT improved the PROM due to a high repetition rate of guided movements in the most neutral and joint-centered position of the pelvis and lower limbs (Kolář, 2002; Žarković and Šorfová, 2017). The findings of this research study are consistent with Vrečar et al. (2013) and indicate that RAGT can be an effective method for improving the PROM of lower extremities in spastic diparesis children with CP.

4.4.2. Interpretation of SCALE results

The following chapter provides discussion on confirmed H6: *'Children with CP will show higher ability to perform selective movements of hip, knee, and ankle joint following RAGT intervention'.*

The latest research suggests that SVMC represents an important factor affecting functional movement tasks including gait, and maybe an indicator of the improvement following therapeutic or surgical interventions (Clowry, 2007; Goldberg et al., 2012, Balzer et al., 2015. Despite clinical findings, SVMC has not been explored as a determinant factor of gait biomechanics in CP children (Fowler et al, 2009). Children with CP have reduced ability to develop skilled intra-limb coordination movements and may develop movement strategies that retain primitive coupled patterns manifesting as an inability to dissociate hip and knee recruitment when ambulating (Fowler et al., 2009; Perry et al., 2010). Coupled movements were also observed in all children with CP that were enrolled in this research study. SVMC is also strongly associated with postural control and stability. Structural brain damage in children with CP can generate an irrelevant motor program leading to abnormal posture (Farmer et al., 2008; Chruscikowski, 2017). Therefore, SVMC of children with CP can be effected either by demanding (e.g. standing, walking) or non-

demanding postural positions (e.g. sitting, lying) (McMulkin et al., 2000; Desloovere et al., 2006). This is the first research study that reported improved SVMC following RAGT in CP children with spastic diparesis. One of the possible explanations why children with CP improved their SCALE scores can be due to posturally non-demanding testing positions. Nevertheless, in this research study, there were no significant changes in sagittal plane joint kinematics in children with CP that would indicate the change of coupling movements among hip, knee, and ankle joints. The findings of this research study indicate that improvement of SVMC in spastic diparesis children with CP can be possible. However, this research study leaves space for improvement in terms of further investigation into how can RAGT improve SVMC in children with CP when ambulating.

4.4.3. Interpretation of 6MWT results

The following chapter provides discussion on confirmed H4: *'RAGT will enhance the ability of children with CP to walk farther distances'.*

The 6MWT is a reliable and valid test for assessing endurance, functional abilities, and outcomes in children with CP. The minimal clinically relevant difference in 6MWT has been estimated as 54 meters (Redelmeier, 1997). Children with CP in this research study had a pre-intervention median value of total distance walked 350 meters which was increased by 75 meters post-intervention to the median value of 425 meters. The findings of this research study are consistent with Beretta et al. (2015) and Beretta et al. (2019) and indicate that RAGT can be an effective method for improving the walking endurance in spastic diparesis children with CP following RAGT.

4.5. Conclusion on scientific question and hypotheses

This research study aimed to answer if 'RAGT can induce a more physiological gait in ambulatory children with CP that would be comparable with healthy children?'. Based on confirmation/rejection of several hypotheses, the key research findings were that RAGT induced more physiological muscle activity and joint kinematics trajectories, more economic energy expenditure in spatiotemporal gait parameters, ability to walk farther distances, increased SVMC ability, and decreased joint contractures. Research findings can be observed from two perspectives:

- findings indicating a more physiological gait due to potential effect on neuroplasticity (sEMG, joint kinematics, SVMC)
- findings indicating functional changes in passive structures and walking capacities that contributed to the overall gait improvement (PROM, spatiotemporal gait parameters, walking farther distances)

RAGT principle is based on intensive, task-specific, and high-repetition-rate of guided movements which contribute to the motor learning process and cortical reorganization (Krishnan, 2019). However, this research study brings to the fore and assumes additional factor that greatly contributes to a more physiological gait pattern of children with CP - centered position of joints. In conditions with impaired motor control, such as in children with CP, joints are in a so-called decentralized position. At the same time, a decentralized joint position also contributes to improper muscle function. The centered joint position allows for optimal loading of the joint in both static and dynamic conditions, as well as it enhances physiological and economic muscle patterns. This is an interesting finding because it indicates that the combination of task-specific guided movements in a high-repetition-rate, and

centered position of joints resulted in a more physiological gait pattern in children with CP. This phenomenon was mostly accented in this research study by a more physiological muscle activation and joint kinematics during gait and static PROM evaluation. Based on findings, it is assumed that RAGT affects motor control by improving functional movement pattern chains which results in a more physiological gait pattern. Indisputably, changes that were observed in gait patterns, SVMC, and walking capacity must reflect the RAGT effect on the CNS. However, such assumption should be confirmed by neuro-imaging methods (e.g. functional magnetic resonance imaging). This study leaves space for improvement in terms of adding neuro-imaging methods which were not available to the PI at the time of this research study.

5. CONCLUSION

CP is considered a condition primarily impacting motor control and movement. Children with CP have varying degrees of muscle weakness, spasticity, decreased SVMC, impaired coordination that limit functional capacity during walking. Because gait abnormalities affect community integration and quality of life, a priority of physiotherapy is to improve gait. After almost three decades RAGT devices are nowadays routine constituent in the gait rehabilitation of adults and pediatric patients. This is the first research study where was shown that RAGT as monotherapy can contribute to a more physiological gait in ambulatory children with CP with spastic diparesis (GMFCS I-III). The most important indicators of gait changes in children with CP were more physiological muscle activity and joint kinematics trajectories followed by increased SVMC and decreased joint

contractures. Additionally, these findings were supported by increased ability to walk the farther distance with more economic energy expenditure. This is the first research study that extended the explanation of RAGT and its contribution to the improved quality of gait pattern by centered joint position. Considering that such changes can be achieved with RAGT as a monotherapy, this method indisputably deserves to be an integral part of pediatric gait rehabilitation. The PI is aware of study limitations such as the small sample size, uncontrolled trial, and lack of long-term follow-up data. For that, there is no tendency from the side of the PI to overemphasize and generalize the study results to a wider spectrum of the CP population. However, this research study provides a foundation on which future studies can be built as RAGT should be investigated over longer periods in different populations to further determine its effectiveness.

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